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NORTH AMERICA

MAYO CLINIC NUMBER

HOUSE COMMITTEE
of the Medical & Dental

PHILADELPHIA AND LONDON
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SYMPOSIUM ON SURGICAL PHYSIOLOGY

APPARATUS FOR RECORDING PHYSIOLOGIC VARIABLES DURING OPERATIONS ON MAN WITH OBSERVATIONS ON CHANGES OF BLOOD PRESSURE DURING RESECTION FOR COARCTATION OF THE AORTA

GEORGE A. HALLENBECK, EARL H. WOOD AND O. THORSON CLAGGETT

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frankly limited to studies in which the subject or patient can be brought to the laboratory. To record physiologic data on patients undergoing surgical procedures it was necessary to design a complete mobile recording oscillograph and associated pick-up units which could be both transported to the operating room and used there without interfering with the operative procedure.

To this end a kymographic slit camera employing 11½ inch (29.2 cm.) photographic paper was built into a table mounted on wheels (Figs 928 and 929). The optical system consisting of light sources, a mirror and several mirror galvanometers, was mounted on top of the table to focus the light beams of the various channels on the camera slit and was covered with a hood of black cloth to permit operation in daylight. Batteries, wiring, the electrical circuits for the oximeter and the cardiostachometer and transformers to vary the intensity of the light sources, together with storage space, were fitted

The camera and table were built by the Waters Loomis Company, Rochester, Minnesota, under the direction of Mr. Richard Jones. The camera was modified from design by Dr. Warren Gibson, of Madison, Wisconsin.

into compartments beneath. Control switches were consolidated on an instrument panel.

In its present form the apparatus can be used to record arterial and venous blood pressure using the strain gauge manometer as described by Lambert and Wood changes of respiratory pressure within the anesthetic mask using a similar strain gauge manometer with an air

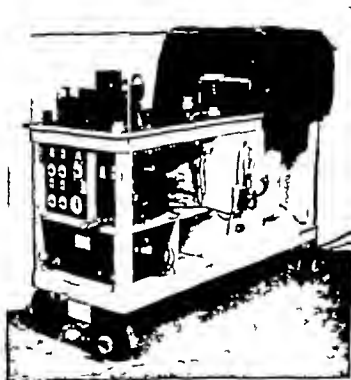


Fig. 275.—Mobile recording oscillograph

system arterial oxygen saturation, using Millikan's compensated current oximeter the electrocardiogram and the pulse rate, using the cardiostachometer* as described by Sturm and Wood and appropriate

The oximeter and cardiostachometer circuits were built by the Waters-Castley Company, Rochester, Minnesota. The oximeter components are obtained from the Coleman Electric Company, Maywood, Illinois.

time signals. The relatively large size of the instrument provides considerable flexibility and other recordings can be added as desired.

Pick-up units to detect the various pressures and transform them into electrical energy must be located near the patient to avoid the loss of manometer frequency which would occur if the liquid-filled lead tubing were unduly long. Accordingly the strain gauge manometers with their connections to the patient and their wash bottle system, the oximeter ear piece, the leads for the cardiometer and



Fig. 228.—Mobile recording oscillograph, showing the associated pick-up units and the cable connecting them to the recording device. See text.

the rubber tubing connected to the anesthetic mask are grouped in a small box, which is placed next to the patient's outstretched arm during the operation. The pick-up units are connected by a shielded cable to the larger recording unit located just outside the operating room. The observer in the operating room communicates with the operator of the recording system by a telephone system.

Through the use of this recording system, records have been obtained of the changes of radial arterial blood pressure which occurred in the course of 4 resections for coarctation of the aorta.

In the first patient radial arterial blood pressure, after the thorax had been opened but before resection of the structure was 160 mm. of mercury systolic and 90 mm. of mercury diastolic. Shortly before the end-to-end anastomosis between the left subclavian artery and the aorta was opened, radial blood pressure was 260/130. Most of this rise of 100 mm. of mercury systolic pressure occurred over a period of several minutes after the proximal segment of the aorta and the left subclavian artery had been clamped. When the anastomosis was

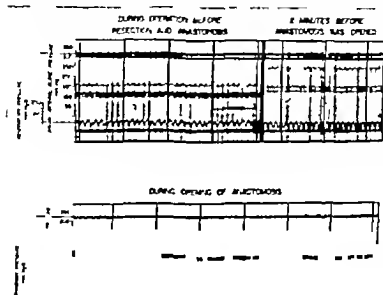


Fig. 229—Respiratory pressure, radial arterial blood pressure and electrocardiogram during resection for connection of the aorta.

opened over a period of thirty-five seconds radial blood pressure fell smoothly and progressively from 265/130 to 185/90 (Fig. 230).

The second patient, a girl aged 11 years, underwent end-to-end

porarily clamped. The record shows a rather dramatic rise of radial arterial blood pressure from 205/110 to 250/120 over a period of seven seconds after the clamp had been applied. The transient fall of

blood pressure that occurred in this case when the distal segment of the aorta was clamped was not encountered in other cases and remains unexplained (Fig 231)

These 3 cases illustrate the marked acute hypertension in the systemic circulation which can occur during surgical procedures for coarctation of the aorta and which can undoubtedly subject the heart to severe strain

In the case of the third patient, end-to-end anastomosis of the aorta was accomplished without the clamping of the left subclavian artery. It is seen that the clamping and later the unclamping of the proximal segment of the aorta resulted in a negligible change of radial blood pressure and pulse rate (Fig 232). This result is to be expected since the aortic structure in this case as in the other cases thus far encoun-

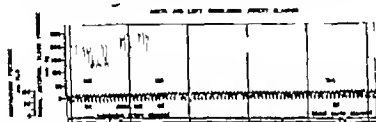


Fig 231—Respiratory pressure and radial arterial blood pressure during resection for coarctation of the aorta. Figures above record of respiratory pressure indicate heart rate per minute; those below respiratory rate per minute.

tered was essentially complete. The radial blood pressure after the thorax had been opened was only slightly higher than that observed while the cutaneous incision was being made. Thus, in this case, the posterolateral incision through the thoracic wall despite its inevitable interruption of some of the collateral blood vessels which compensate for the aortic structure produced only a slight rise of radial arterial blood pressure. Opening of the anastomosis over a period of ninety seconds resulted in a gradual fall of blood pressure from 165/97 to 115/70 with a rise of pulse rate from 126 to 135 beats per minute.

Again in the case of the third patient, end-to-end anastomosis of the aorta was accomplished without the clamping of the left subclavian artery. It is seen that the clamping and later the unclamping of the proximal segment of the aorta resulted in a negligible change of radial blood pressure and pulse rate. As in the third case, the opening of the thorax was associated with only a slight rise of radial blood pressure. When the anastomosis was slowly opened over a period of sixty sec-

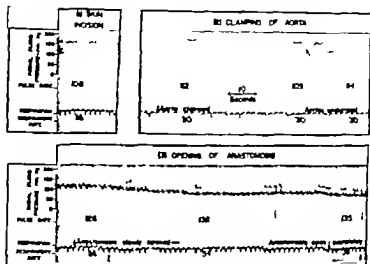


Fig 131—Radial blood pressure, pulse rate, respiratory pressure, and respiratory rate during reaction for constriction of the aorta

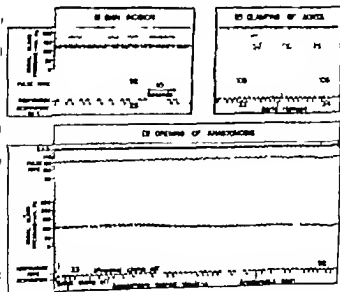


Fig 132—Radial blood pressure, electrocardiogram, pulse rate, respiratory pressure, and respiratory rate during reaction for constriction of the aorta

onda, radial blood pressure gradually fell from 197/88 to 140/75. In this instance pulse rate was almost unaffected (Fig. 233).

The important changes of radial blood pressure during resection for coarctation of the aorta in these 4 cases are summarized in table 1. In the 3 cases in which the left subclavian artery as well as the aorta was clamped during establishment of the vascular anastomosis the greatest hypertension developed during the procedure. The fall of radial systolic blood pressure when the anastomosis was opened varied among these four cases from 35 to 80 mm. of mercury. In the cases in which more than one set of figures is given, bleeding occurred when the anastomosis was first opened and reclamping was necessary in order to allow placement of a hemostatic suture. Therefore in all but the last group of values for each patient, the fall of blood pressure when the anastomosis was opened was augmented to some degree by

tolic blood pressure when the anastomosis was opened varied from 35 to 80 mm. of mercury. These values confirm those obtained in the 4 cases in which more accurate measurements were made.

COMMENT

Gross has reported an instance in which a patient expired during resection for coarctation of the aorta when his blood pressure fell to very low levels as the anastomosis was opened and failed to recover despite the fact that the anastomosis was re-clamped and supportive measures were undertaken immediately. As a result of this experience he has recommended that the anastomosis be opened slowly over a period of approximately ten minutes while the operating table is in slight Trendelenburg position and blood is being administered intravenously to the patient. We have not yet encountered a case in which the profound fall of blood pressure noted in Gross's case has occurred. The possibility must be always kept in mind, however, and guarded against by careful, slow opening of the anastomosis while frequent determinations of blood pressure are made.

The severe acute hypertension which occurred in the 3 cases in which the left subclavian artery was temporarily clamped and which was not encountered in 3 other cases in which this vessel remained uninterrupted warrants the recommendation that whenever possible the operation for coarctation of the aorta be carried out with the proximal aortic clamp placed distal to the subclavian artery. In many cases, however, this procedure will be anatomically impossible because

TABLE 1

RESULTS OF IMPROVED CLAMPING OF BLOOD PRESSURES IN THE RADIAL ARTERY OBSERVING DURING SURGICAL RESECTION FOR COLLECT FROM THE AORTA

Age	Type of Operation	Blood Pressure in the Radial Artery mm. of mercury									
		Depressing of Operation	If blood pressure Pressure	Clamping of Vessel Proximal to Structure				At Opening of Anastomosis			
				Before	Immediately after	Flow		Before	After	Pulse	
						Systolic	Diastolic			Systolic	Diastolic
60	BC A	170/85	900/100	100/100	400/100†	40	0	415/110	185/90	90	30
11	A A	100/85	630/100	604/110	430/100†	65	10	415/114	165/95	90	47
25	A A	170/100	100/107	187/107	185/107‡	0	0	185/114	180/97	55	45
30	A A	170/100	100/107	187/107	185/107‡	0	0	172/108	185/98	37	60
30	A A	180/100	100/100	180/100	180/100	10	0	185/97	115/70	20	47
30	A A	180/100	100/100	180/100	180/100	0	0	185/90	180/90	35	10
30	A A	180/100	100/100	180/100	180/100	0	0	187/90	160/75	37	15

BC A = end-to-end anastomosis between left subclavian artery and aorta

A A = end-to-end anastomosis between proximal and distal segments of aorta.

† Both the left subclavian artery and the aorta were temporarily clamped

‡ The aorta proximal to the structure but distal to the left subclavian artery as clamped

of the proximity of the aortic structure to the origin of the subclavian artery

When the posterolateral thoracic incision is made on a patient who has coarctation of the aorta, it is evident from the intense vascularity of the region that many collateral blood vessels are cut. The fact that radial arterial blood pressure underwent only a modest rise in the 8 cases in which recordings were obtained during this procedure might suggest at first glance that the collateral blood supply thus interrupted is a small part of the total available blood supply. This may be the case, but these data alone do not permit such a conclusion, because several factors which may also affect blood pressure remain uncontrolled. Prominent among these are the loss of blood which occurs at this time, the effect of continued anesthesia and the possibility that vasomotor regulation of blood pressure may be occurring to stabilize blood pressure in the face of ligation of collateral vascular channels.

SUMMARY

By means of a mobile multiple channel oscillograph with associated pick-up units, which is suitable for recording physiologic variables during operations on man, observations were made of the changes of blood pressure in the radial artery during resection for coarctation of the aorta. On the basis of these observations it is recommended that, whenever possible, the proximal aortic clamp be placed distal to the subclavian artery to avoid the severe hypertension which occurred in 8 cases in which this procedure was not followed.

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SURGICAL TREATMENT OF IMBALANCE OF THE EXTRA OCULAR MUSCLES PHYSIOLOGIC ASPECTS

ALFRED DEH FRANKLIN

It is assumed that the same general physiologic principles apply to all surgery. However application of these principles in the several fields of surgery varies. In one field eradication of disease is the object, while in another field correction of dysfunction or restoration of normal function is stressed. Surgery for imbalance of the extra ocular muscles is orthopedic (corrective) in nature. This is in contrast to the idea of mere cosmetic improvement. Since in operations for imbalance of the muscles of the eye the surgeon cannot be satisfied with mere cosmetic improvement but must strive to attain a real cure or restoration of function, he must have a clear understanding of the physiology of the extra-ocular muscles. To me, the greatest advances in surgery on the muscles of the eye in the past twenty-five years have been dependent on such understanding; these advances have taken the form of refinement of diagnosis and simplification and rationalization of operative procedures. In my opinion these advances have been based on a better understanding of the physiology of ocular motility.

To be sure ophthalmologists know that it is often difficult, and sometimes impossible, to make an exact diagnosis in cases of imbalance of the extra-ocular muscles. Nevertheless success in treatment of the imbalance is based on correct diagnosis. After refined differential diag-

to arrive at definite conclusions. The degree of imbalance often changes from one observation to the next.

After all the diagnostic data are assembled it may be evident that treatment should be surgical. If so careful study of the existing state of function of the eye muscles is a great aid in selecting the type of operation to be performed.¹¹ When eyes are made to function properly their visual axes are parallel or, to use the common expression, the eyes are "straight." Therefore when several types of surgical procedure are available for straightening a pair of eyes, the best is that which will assure restoration of function. However usually there is no hurry to operate.

WHEN TO OPERATE

Factors which must be considered in the decision of when to operate are as follows: age of the patient, previous treatment, whether or not the condition is improving, accessibility of the patient for prolonged nonoperative treatment, the personality of the patient, the ability of the patient and his family to co-operate in the treatment, and the social and economic status of the patient and his family.

The age of the patient is not as important as formerly it was thought to be. Modern procedures, such as improved methods of diagnosis and general anesthesia, the recession operation, simplified resections and the use of gut sutures have made it possible to operate safely and accurately even at an early age. Our youngest age for operation is about three years. In dealing with children it is well to remember that the young, growing mechanism has an inherent tendency to correct itself with minimal surgery. Many times unilateral recession of a rectus medialis muscle has corrected convergent strabismus in a child when eventual bilateral recession seemed indicated. If the patient is an adult, minimal surgery rarely is enough because the deformity has become fixed. It seems to me that the surgeon, in operating on the extraocular muscles, must be "radical and yet accurate" and that he must try to visualize the underlying physiologic condition and its pathologic changes.

If imbalance is variable, particularly if it is improving, operation should be deferred. It is granted that many patients can be cured by rather prolonged nonoperative treatment. Sufficient trial of nonoperative measures should include a period of six months to two years, depending on the circumstances. I am heartily in favor of orthoptic

— — — — — 113 — — — — — however, orthoptic

than has been the custom, surgery should be resorted to earlier. Spontaneous recovery of fusion and of stereopsis often are noted after surgical correction when no other treatment has been given.

When the diagnosis is obvious and proper nonoperative management has been tried sufficiently but the imbalance has not improved or has become more marked, operation without delay is indicated. To delay is only to make matters worse. Some patients, particularly children suffering from severe strabismus, come long distances to the ophthalmologist and cannot be kept under prolonged observation and nonoperative treatment. In these cases, if strabismus is severe, it is

often advisable to operate and put the eyes in such position that they will help themselves to straighten.

A few lines farther the possibility was entertained that prolonged orthoptic training may not be possible in a given case. Circumstances which interfere with adoption of orthoptic training are likely to be found in the aforementioned personality of the patient (and of one or more members of his family) or in his economic status. The patient may be unco-operative either by nature or by necessity.

OPERATIONS FOR BILATERAL DEFECTS

Ophthalmic surgeons have a natural aversion to operating on both eyes at one sitting. It is probably best to operate on only one eye and then at a later date to operate on the other. However, when patients come from long distances and are unable to return for further treatment it may be necessary to operate on the second eye a few days after operation on the first. Whether to operate on both eyes at all or only on one is also determined, of course, by the severity of the defect and whether it is bilateral. When a bilateral defect exists my impression is that it is better to correct both eyes eventually rather than to unbalance the eyes in an effort to obtain correction by operation on only one eye. Again, restoration of normal function rather than mere cosmetic straightening is of major importance.

In complicated cases of muscular imbalance such as combined lateral and vertical defects or mixed bilateral involvement, I believe that operation for the outstanding defect should be performed first. This leaves the action of other muscles, concerning which doubt exists, or the other eye for subsequent observation and if they fail to undergo adjustment, possibly for operation later. Often when operation is performed on the worst offending muscle, muscles or eye the lesser offender or the other eye will adjust itself and further operation is not needed or may be much less extensive than originally

procedure fol

inability to
straighten and hold straight, by surgery eyes with anomalous retinal
correspondence. I have found this to be true only of eyes which have
extreme amblyopia and marked eccentric fixation. When deviating

eyes fixate properly. I have found that they respond satisfactorily to cosmetic surgery regardless of anomalous correspondence. However when deviating eyes fixate eccentrically I have found that they do not remain straight after cosmetic surgery and that they have a marked tendency to turn toward their previous position of deviation.

IMPORTANCE AND CHARACTERISTICS OF THE VARIOUS TISSUES ENCOUNTERED

The importance and characteristics of the various tissues encountered during an operation on the extra-ocular muscles should be considered. The conjunctiva, or protective coat of the globe is the point of entrance and the means of closing the surgical wound. It should be incised cleanly and widely and at the proper points, so that it can be smoothly replaced and evenly closed with a delicate suture. Failure to do these things invites a clinging wound with excessive granulation and poor healing. Improper conjunctival excitation may adversely affect the result of an operation on ocular muscles and vice versa.

Tenon's capsule is a key structure in operation on muscles of the eyes. This fact has been called to our attention by Jarnson and by Berens and Romaine. Jarnson states that Tenon's capsule could be utilized to reinforce poorly developed muscles or that it could be altered so as to lessen the action of hypertonic muscles. Berens and Romaine call attention to the necessity for preservation and conservation of Tenon's capsule; they said that muscles should be covered with Tenon's capsule while the surgeon is operating so as to minimize postoperative adhesion of individual muscle to the sclera. Such adhesion when excessive tends to defeat operative effort. With the observations of these authors I am in thorough accord.

It goes without saying that the type and development of tendon and muscle encountered materially affect the decision as to what to do and how much to do surgically; the tendon and muscle. Preoperative ideas concerning the nature of these structures may have to be changed at the time of surgical exposure. The exact power or tension of muscles can be determined only at operation. Frequently anomalous insertions and attachments of tendon and muscle to the sclera are encountered and have to be corrected. I have encountered insertions at abnormal distances and abnormal angles from the corneal

Unless due recognition is given to these anomalous conditions and proper disposal of them is made results will not be good

RADICALNESS OF THE OPERATION

In operating we must always have due regard for minimal trauma to tissue and yet we must be radical enough in our efforts to attain our objectives. Often the most radical surgery is the best and least traumatizing. In my earlier years trying to assume minimal damage I handicapped my efforts by small stingy incisions and inadequate dissection or exposure of essential structures in the field of operation. This fault I have observed often in others. Before reconstruction and alteration of tendons and muscles can be properly carried out, it is necessary to visualize freely and to study the tissues to be altered. Incisions heal crosswise and not lengthwise. Therefore a long incision permitting wide exposure and free visualization is best. As pointed out by Jamieson Kirby and others the condition of tissues as found at operation often determines or alters the type or extent of the surgery to be performed. If we do not "open up" wide enough, we cannot see these tissues. Again I repeat in reconstructing tendons and muscles we must be radical enough to attain our objectives. It has been my experience that overcorrections of muscular defects have been very few indeed whereas undercorrections or partial successes have been far too common. Personally I should much prefer an occasional overcorrection and to reoperate if it than to wonder what to do next for frequent halfway or partial results. In truth, many postoperative conditions which are somewhat overcorrected in our opinion as ophthalmic surgeons, are in fact most acceptable to the patient and family whereas many conditions which to us are somewhat undercorrected are certainly unsatisfactory to the patient and the family as well as to us.

In resection of the rectus muscles, how much shall we resect? I have cause to feel that we should resect enough to take up the "slack" or "give" in the muscle. With the muscle completely freed from all global and conjunctival attachments and held forward on the muscle hook, the Prince forceps is shoved backward until the muscle in the forceps is under distinct tension. Measurement from the hook to the back of the forceps, where the sutures go usually shows that in the case of the lateral rectus muscle from 10 to 11 mm. of tendon has been resected. In the case of the rectus medialis muscle this measurement is from 8 to 10 mm. in the case of the inferior rectus muscle from 5 to 6 mm. in the case of the superior rectus muscle from 5 to 6 mm. If

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IMPORTANCE AND CHARACTERISTICS OF THE VARIOUS TISSUES ENCOUNTERED

The importance and characteristics of the various tissues encountered during an operation on the extra-ocular muscles should be considered. The conjunctiva or protective coat of the globe is the point of entrance and the means of closing the surgical wound. It should be incised cleanly and widely and at the proper points, so that it can be smoothly replaced and evenly closed with adequate sutures. Failure to do these things invites sloughing wounds with excessive granulation and poor healing. Improper conjunctival cleavage may adversely affect the result of an operation on ocular muscles and vice versa.

Tenon's capsule is a key structure in operation on muscles of the eyes. This fact has been called to our attention by Jamieson and by Berens and Romaine. Jamieson stated that Tenon's capsule could be utilized to reinforce poorly developed muscles or that it could be altered so as to lessen the action of hypertonic muscles. Berens and Romaine called attention to the necessity for preservation and conservation of Tenon's capsule; they said that muscles should be covered with Tenon's capsule while the surgeon is operating, so as to minimize postoperative adhesions of tendon and muscle to the sclera. Such adhesions when excessive tend to defat operative efforts. With the observations of these authors I am in thorough accord.

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ideas concerning the nature of these structures may have to be changed at the time of surgical exposure. The exact power or tension of muscles can be determined only at operation. Frequently anomalous insertions and attachments of tendons and muscles to the sclera are encountered and have to be corrected. I have encountered an-

— but none at abnormal angles from the corneal
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Unless due recognition is given to these anomalous conditions and proper disposal of them is made results will not be good.

RADICALNESS OF THE OPERATION

In operating we must always have due regard for minimal trauma to tissue and yet we must be radical enough in our efforts to attain our objectives. Often the most radical surgery is the best and least traumatizing. In my earlier years, trying to assure minimal damage I handicapped my efforts by small, stingy incisions and inadequate dissection or exposure of essential structures in the field of operation. This fault I have observed often in others. Before reconstruction and alteration of tendons and muscles can be properly carried out, it is necessary to visualize freely and to study the tissues to be altered. Incisions heal crosswise and not lengthwise. Therefore a long incision permitting wide exposure and free visualization is best. As pointed out by Jameson, Harby and others, the condition of tissues as found at operation often determines or alters the type or extent of the surgery to be performed. If we do not "open up" wide enough, we cannot see these tissues. Again I repeat, in reconstructing tendons and muscles we must be radical enough to attain our objectives. It has been my experience that overcorrections of muscular defects have been very few indeed, whereas undercorrections or partial successes have been far too common. Personally I should much prefer an occasional overcorrection and to reoperate for it than to wonder what to do next for frequent halfway or partial results. In truth many postoperative conditions which are somewhat overcorrected, in our opinion as ophthalmic surgeons, are in fact most acceptable to the patient and family, whereas many conditions which to us are somewhat undercorrected are certainly unsatisfactory to the patient and the family as well as to us.

In resection of the rectus muscles, how much shall we resect? I have cause to feel that we should resect enough to take up the "slack" or "give" in the muscle. With the muscle completely freed from all global and conjunctival attachments and held forward on the muscle hook, the Prince forceps is shoved backward until the muscle in the forceps is under distinct tension. Measurement from the hook to the back of the forceps, where the sutures go, usually shows that in the case of the lateral rectus muscle from 10 to 11 mm. of tendon has been resected. In the case of the rectus medialis muscle this measurement is from 8 to 10 mm. in the case of the inferior rectus muscle from 5 to 6 mm. in the case of the superior rectus muscle from 5 to 6 mm. If

the muscle is paralyzed and flabby these measurements will be several millimeters higher. Such radical resections really got results. I have the feeling that small resections usually are failures. Rarely in my experience has even slight strabismus been corrected by a single resection or recession operation in adults. It is usually necessary to operate on more than one muscle of the same eye or on the fellow eye.

In recessing rectus tendons, I have found small recessions to result in failure. The medial rectus muscle I recess 5 mm. no more and no less. The external rectus muscle due to its long arc of contact with the globe is difficult to weaken. I recess 6 mm. when I perform the recession operation on this muscle. The inferior rectus and the superior rectus muscles I recess from 4 to 5 mm.

Operations on the oblique muscles have been described by Wheeler, Berens and Loutfallah, Dunnington, White, Gailbor, Hughes, Wagnan and Berke. There is an increasing, and I think correct, tendency to perform radical reconstruction of these muscles so difficult to operate on. The oblique muscles are difficult to treat surgically because of their obscure and peculiar anatomic relationships. In operating on them one must be persistent in dissection and carry it on to the point at which these muscles are as completely freed and viable as the rectus muscles are when they are operated on. When this is done the oblique muscles can be easily altered at will. At least, I know this to be true of the inferior oblique muscle and Berke has shown that it is likewise true of the superior oblique muscle.

very disappointing. Results obtained from the posterior or global approach have been much better especially since I have been recessing the tendon. Recently I have been setting the "completely" freed tendon of the inferior oblique muscle forward on the horizontal meridian of the globe to a point 6 to 7 mm. posterior to the middle of the point of attachment of the rectus lateralis muscle. This places the attachment of the inferior oblique tendon close or slightly posterior to the end of the theoretic horizontal axis of elevation and depression

I have found in the few cases in which I use the Callahan procedure that this method of reducing the action of the inferior oblique

muscle is very successful. I recommend that it be given a trial. To allow the inferior oblique muscle to become attached anywhere on the posterior inferior quadrant of the globe, as it will become attached after tenotomy or tenectomy seems to me to invite failure. In anchoring the inferior oblique tendon to the sclera, I use one suture of plain catgut, no. 0000 tied completely around the tendon and then woven through it and left buried.

I regard tendon transplantation to be well worth trying in the treatment of paralysis of the rectus muscles, particularly in the case of the lateral rectus muscle. In my experience, excellent motion is obtained in the paralyzed field in about 50 per cent of cases in which the aforementioned procedure is performed. When the transplants fail to act, the eye will be cosmetically straight because of the "extensive" resection performed on the paralyzed muscle and the partially crippling recession performed on the opposing muscle. In the case of a paralyzed rectus lateralis muscle, I resect the paralyzed muscle a maximal amount—15 to 18 mm.—and recess the opposing rectus medialis muscle 6 mm. The technique of the operation has been described in several excellent articles by various authors.¹⁻¹²

POSTOPERATIVE MANAGEMENT

The immediate postoperative management of patients who have undergone operations on muscles of the eyes seems to be an individual problem. Each surgeon has his own ideas and routine which he feels return to good condition the eyes which have been subjected to operation. It seems to me that eyes which have been operated on recover very satisfactorily regardless of which postoperative regimen is followed. If an eye on which an operation has been performed is kept clean "outside" and reasonably quiet for a few days, it will progress satisfactorily. Dr. Edward Jackson once told me that if the eyelids and eyelashes were kept clean adequate drainage would be established naturally. In other words, irrigation of the eyes is unnecessary. In recent years I have followed this advice. At the Clinic our postoperative care is simple, based on minimal disturbance of a part recently operated on. The eyelids and eyelashes are cleansed, some form of ocular antiseptic agent is instilled and pads are applied. The eyes are not irrigated. I believe that it is better not to interfere with the chemical content of the conjunctival cul-de-sac. Our postoperative reactions have been definitely less since we ceased to use postoperative irrigation of the conjunctival cul-de-sac. When marked reactions are en-

countered, I have found that the intramuscular injection of boiled

undergone operations on muscles of the eyes is of more interest. There is no doubt in my mind that orthoptic treatment which is intelligently directed must be of definite value in the postoperative care of such patients. My use of such treatment has been limited, but enough to convince me of its value. Orthoptic treatment to cure some muscular defect may make operation unnecessary and its use to assist in refining the diagnosis in all cases of muscular defects is of unquestioned value. Postoperative orthoptic treatment should be ideal to complete a cure in selected cases, but not in all. In adults, particularly and also in children in the presence of postoperative diplopia and persistent fusion "inability" I think orthoptic treatment should be studiously avoided. Orthoptic treatment in such cases is not only futile in my observation but also tends to fix the diplopia and to keep the patient confused and unhappy. Postoperative diplopia and fusion inability I believe are managed best by the absence of orthoptic treatment. It is sometimes best to let sleeping dogs lie. I have seen a considerable number of patients who had so-called horror of fusion with eyes that had been intensively treated orthoptically after surgical treatment of muscles of the eyes. These patients have been very unhappy people. I think the best treatment for postoperative diplopia among patients who have undergone operation on the ocular muscles is to ignore it, unless the diplopia responds immediately to orthoptic treatment.

SUMMARY

Corrective surgical treatment of the extra-ocular muscles is orthopedic in nature. Its success is based largely on a clear understanding of the physiology of ocular motility and its pathological variations. The physiologic basis applies equally to diagnosis and to treatment, surgical and nonsurgical.

A refined differential diagnosis is the first requisite of extra-ocular muscle surgery. In deciding to operate one should be guided not so much by the age of the patient as by the degree and nature of the strabismus, the condition of the visual apparatus and the response or lack of response of the latter to nonoperative treatment.

In reconstructing tendons, while due respect should be paid to tissue "one must nevertheless be radical enough to attain the desired objective.

Exact measurement should be used in altering tendon insertions on the sclera plain gut sutures are preferable for securing scleral anchorage, and intramuscular injection of boiled whole milk has been found useful in controlling undue postoperative reaction.

It is felt that the surgeon is more likely to undercorrect than to overcorrect in operating for strabismus.

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PHYSIOLOGIC DISTURBANCES UNDERLYING THE DEVELOPMENT OF EARLY POSTOPERATIVE ATELECTASIS AFTER LOBECTOMY

WILLIAM D. SNYBOLD

INTRODUCTION

COLLAPSE of a remaining lobe or lobes after removal of a diseased pulmonary lobe or lobar segment is the most frequent complication occurring in the early postoperative period.^{1, 2, 3, 4, 5} It is a serious complication that, if the mechanisms of its production are properly understood commonly can be prevented and one which when fully developed must be treated promptly to avoid the serious sequelae of pneumonia, pulmonary abscess, bronchiectasis in the affected lobe and empyema of the affected pleura. The protection of the remaining lung from postoperative suppurative disease its inherent immediate dangers and its damaging sequelae is dependent on the prevention or the immediate relief of lobar collapse. The maintenance of well-expanded lobes is likewise the most important factor in the prevention of postoperative pleural complications⁶ that can threaten life delay convalescence and permanently impair pulmonary function by fixation of the lung and thoracic cage.

An analysis of the factors which contribute to the development of lobar collapse after lobectomy must be based on a consideration of the physiologic mechanisms of pulmonary ventilation bronchial function and cough. Though, occasionally anatomic causes are present to account for postoperative lobar collapse⁷ functional disturbances of the ventilatory bronchial secretory and cough mechanisms are primarily responsible. It is the purpose of this paper to attempt an enumeration of these disturbances of normal function to consider in detail the factors underlying them, and finally to offer suggestions as to how such derangements may be minimized and atelectasis may be reduced in frequency or be dealt with promptly and effectively so that serious permanent sequelae may be avoided.

DISTURBANCES OF PULMONARY VENTILATION AFTER LOBECTOMY

It has been known for many years that rather profound disturbances of pulmonary ventilation follow abdominal operations. A number of workers⁸ have made accurate measurements of the effect of laparotomy on vital capacity tidal air complement and supple-

mental air and the respiratory rate during the early postoperative period. They have shown that vital capacity is reduced as much as 58 per cent on the first postoperative day (Fig. 234) and that the respiratory rate is greatly accelerated and the tidal volume reduced by 20 per cent or more² (Fig. 235). These changes have been shown to be greater in upper abdominal incisions than in lower abdominal incision and to have a close correlation to the development of post operative atelectasis.

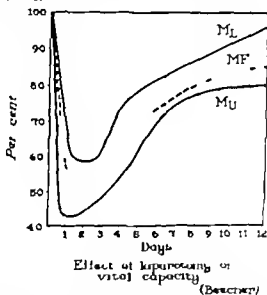


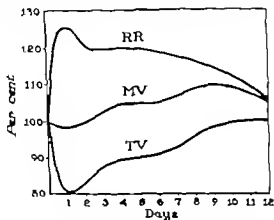
Fig. 234.—Effect of laparotomy on vital capacity. M_L , Average postoperative vital capacity in percentage of normal after lower abdominal incisions. M_U Same after upper abdominal incisions. M_F Same for all cases. (Redrawn from Bauer: *II A. J. Clin. Investigation*, Vol. 12.)

Comparable studies of the measured effects of thoracotomy on pulmonary ventilation has not been published, though there is need for

degree. Though with rapid shallow breathing the tidal volume is small and

nificantly to intrapulmonary conditions favoring bronchial obstruction and atelectasis. This will be dealt with more fully in a subsequent paragraph.

Beecher measured the effect of laparotomy on complementary and supplemental air as an index of the efficiency of the muscles of forced inspiration and expiration (Fig 233). He found a striking change in both series and a 20 per cent greater reduction of complementary air in upper abdominal incisions in males than in females. As is the case with the other measurements of ventilatory function, the reduction



Post-operative rapid shallow respiration after laparotomy
(Beecher)

Fig 233—Changes in respiratory rate (RR), minute volume (MV) and tidal volume (TV) after laparotomy in terms of percentage of normal (Redrawn from Beecher H. A. *J Clin Investigation*, Vol 18)

was considerably greater in upper abdominal incisions than in lower abdominal incisions.

Clinical observation lends strong support to the idea that similar changes of even greater magnitude occur after thoracotomy and, furthermore these changes, except for the respiratory rate are much greater on the side of the thoracotomy than on the opposite side. Thus, ventilation of the remaining lobe or lobes after lobectomy is diminished even more than that of the opposite lung. This is a very significant factor in explaining the much greater frequency of lobar collapse on the same side than on the opposite side. In an analysis of 23 cases of lobar atelectasis complicating pulmonary lobectomy Gray

found only 1 case in which a lobe of the opposite lung was involved. In 51 cases of atelectasis occurring in a series of 100 unselected cases in which lobectomy was performed at the Mayo Clinic collapse occurred on the opposite side alone only once and that was due to retention of bronchial secretion while the patient was in lateral position on the operating table. The atelectasis cleared spontaneously during the first twenty-four hours of the postoperative period. No doubt there

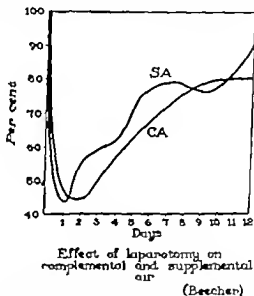


Fig. 128.—Effect of laparotomy on complementary (CA) and supplemental (SA) air (Redrawn from Beecher H. A. *J. Clin. Investigation*, Vol. 12.)

are other important factors, and these will be considered in subsequent paragraphs.

FACTORS CONTRIBUTING TO POSTOPERATIVE DISTURBANCES OF PULMONARY VENTILATION

Motion of the thoracic wall is directly interfered with as a result of trauma to some of the muscles of respiration and of accessory respiration in the making and closing of the surgical incision. Thoracotomy for lobectomy involves a long incision in the thoracic wall with or without excision of segments of one or more ribs. The most common approach is a posterolateral one through the bed of the fifth, sixth

or seventh rib. Some splinting of the thoracic wall on the side of the incision occurs in every patient during the early postoperative period. This is the result of reduction of function of the several respiratory muscles, primary and accessory which have been damaged by the incision and the function of which is greatly influenced by reflexes initiated by pain in the incision by the constricting effect of the surgical dressing and by the position of the patient in bed.

Trauma to the structures in the thoracic wall cannot be avoided, but it can be minimized by strict adherence to generally accepted principles of good surgical technique. Pain in the region of the incision after thoracotomy is probably of greater intensity and longer duration in the average case than it is after laparotomy. It is greatly to be desired that this pain be reduced or controlled not only because of humanitarian considerations, but because of the important role pain plays in reduction of thoracic excursion and therefore pulmonary ventilation and in interference with an effective cough. Coughing is a painful experience after thoracotomy and unless the pain can be sufficiently well controlled to permit good ventilation and a vigorous cough retention of bronchial secretion, bronchial obstruction and lobar collapse are almost inevitable sequelae.

There are a number of more or less controllable factors that bear on the intensity and duration of the pain. When the incision is made unnecessary trauma to the intercostal nerve trunks should be avoided. Wishing to eliminate the crushing force applied to the intercostal bundles by the standard rib spreaders, my colleagues and I tried an instrument that applied force directly to the ribs through multiple small pins placed through the bone. This was unsatisfactory, however, for the strength of the bone was not sufficient to withstand the distribution of force and fracture resulted. Perhaps the main trunk of the intercostal nerve is sufficiently well protected by the inferior margin of the corresponding rib so that spreaders cause no real damage, but this seems unlikely.

Avoidance of inclusion of the intercostal nerve trunks in the suture line during closure of the thoracic incision is certainly desirable on theoretical grounds though the multiplicity of factors influencing pain including individual variations of the threshold of pain, make evaluation of the technique of closure from this standpoint difficult. A number of satisfactory ways of approximating the ribs in closure of the incision while avoiding the intercostal nerve trunks have been devised and are being practiced.

Injection of anesthetic substances into several intercostal nerve

trunks above and below the level of the incision under direct vision while the thorax is open has been recommended and tried. Johnson has recommended crushing the nerves rather than injecting them. The resulting numbness is as annoying to some patients as their pain probably would have been. However, it is a procedure that may have merit in selected cases.

Pain can perhaps be lessened by attention to some of the technical points in the operative procedures that have been mentioned in the previous paragraphs, but further measures are necessary in the immediate postoperative period after the patient regains consciousness. Drugs which most effectively control pain also reduce the sensitivity of the mucous membrane of the tracheobronchial tree and therefore interfere with the cough reflex. The desired goal in the use of analgesics in these patients must be the provision of reasonable comfort without depression of the cough reflex. Meperidine hydrochloride (demerol) has less depressant action on the cough reflex than opiates, but is commonly not as effective an analgesic. In clinical practice, however, it has proved satisfactory in the relief of pain. There is another action which gives it an advantage over the derivatives of opium. Whereas the latter when given in therapeutic doses, cause bronchial constriction, demerol causes relaxation of the bronchial musculature and dilatation of the smaller bronchi and bronchioles.¹ For these reasons it seems to have a rational place in the postoperative care of patients who have undergone lobectomy. Reference will be made to this point again in the discussion of disturbances of bronchial function.

For obvious reasons a tight circular thoracic dressing is to be even more carefully avoided after thoracotomy than a tight abdominal bander after laparotomy. Such a dressing can and commonly does contribute to further reduction of pulmonary ventilation by its mechanical limitation of inspiration. A dressing that merely covers the incision and is fixed to the skin with adhesive tape which is not of sufficient length or extent to interfere with respiratory motion is the most desirable one.

The principles of good postoperative care generally apply in the handling of patients after lobectomy. Movement of the lower extremities and frequent change of position in bed should be insisted on. After lobectomy the patient is more comfortable in a semisitting position. Diaphragmatic motion is aided thereby. The patient should spend some time on both of his sides as well as on his back, but the side from which the lobe was removed should be kept up most of the time to permit the widest possible respiratory excursions on the lobectomized

side and to encourage drainage of bronchial secretions from this side by gravity flow

It is apparent that the position of the patient in bed can be a factor which contributes to a postoperative disturbance of pulmonary ventilation and of the proper drainage of bronchial secretions. By proper attention to this point undesirable effects can be lessened if not avoided

There is another factor in pulmonary ventilation which may have a bearing on postoperative disturbances which contribute to lobar collapse. The role of the diaphragm in ventilatory function is so well known that a discussion of it seems unnecessary. More will be said later about its role in the cough mechanism. Because interruption of a phrenic nerve results in paralysis and elevation of the corresponding hemidiaphragm, section or crushing of a phrenic nerve has frequently been done during the course of lobectomy for the purpose of obliterating more completely and rapidly the pleural space previously occupied by the diseased lobe or lobes. In this series of patients interruption of the phrenic nerve was most commonly carried out when more than one lobe or an upper lobe was removed. In the group of 100 patients previously referred to 12 underwent phrenicorrhaphy at the time of lobectomy. Five of these 12 (42 per cent) experienced lobar collapse during the early postoperative period, but in 2 cases it seemed to be due to external compression by fluid and air rather than to retention of secretions, bronchial obstruction and collapse. On the basis of these few cases, one cannot definitely show an adverse effect of phrenicorrhaphy, though on theoretical grounds, it seems objectionable. It is known that the diaphragm will rise to accommodate a smaller lung in the absence of interruption of a phrenic nerve and its active function in the early postoperative period is desirable for maximal ventilation and for effective cough.

DISTURBANCES OF BRONCHIAL FUNCTION

The mucous glands in the normal tracheobronchial tree produce a small amount of mucoid secretion which keeps the mucosal surface moist and which aids in the removal of particulate matter brought into the lungs in the inspired air. The mucus is a vehicle in which these particles are carried to the pharynx by the combination of ciliary action and cough. In most inflammatory lesions of the lungs and bronchi there is a radical departure from normal in the quantity and character of this secretion. In suppurative disease of the lungs, such as lung abscess and bronchiectasis, bronchial secretion is usually

copious and thick. It is in this group of patients that early postoperative lobar collapse is most frequent in our own experience and in that of others.⁷⁻⁹ Though very excessive quantities of sputum cannot be correlated with a higher incidence of postoperative pulmonary collapse,⁷ patients without an abnormal quantity rarely experience atelectasis after any operation whether it is thoracic or abdominal.¹⁰ In this connection it is noteworthy that after intrathoracic procedures for extrapulmonary lesions such as mediastinal or esophageal tumor postoperative lobar collapse is rare even though many of the factors which limit ventilation are present.

In an attempt to reduce the quantity of bronchial secretion and lessen bronchial infection before lobectomy is undertaken my colleagues and I have recently employed not only postural drainage exercises but the intrabronchial administration of penicillin by nebulization. This has been quite effective in reducing the volume of sputum and in changing its character from an offensive one to a rather innocuous mucoid one in many cases, but the incidence of postoperative lobar collapse has not been greatly affected. It is very unusual to be able to reduce the volume of sputum to zero by these methods, and apparently a sufficient quantity remains to cause collapse if other contributory factors are in operation.

In order to reduce the viscosity of pulmonary secretions, our patients are put in a croup tent which is equipped with a steam kettle and they are kept there as long as a productive cough persists. It has been our impression that this has contributed to the comfort of the patient as well as to the ease with which he effectively raises sputum.

Whereas it commonly has been believed that normal ciliary action is absent in many inflammatory bronchial lesions and as a result, the secretions are not moved centrally in the lung but accumulate to the point of complete obstruction in the bronchi with consequent atelectasis. Halding has expressed the view that ciliary action is present under these circumstances and that it plays an important role in the pathogenesis of lobar collapse. His experimental observations, which are novel and pertinent, lend support to his thesis and throw new light on previous experimental and clinical observation on pulmonary collapse. His approach affords a rational explanation for a number of previously recorded observations that seemed isolated or contradictory.

Knowledge that changes in length and diameter of bronchi occur with changes in the ventilatory cycle is not new. Douglas and Haldane demonstrated such changes by measurements of dead air space and

by bronchographic methods, Heinbecker showed that bronchi and bronchioles are widest at the end of full inspiration and narrowest at the end of expiration (Fig. 237). Such changes are observed by the bronchoscopist during the course of every bronchoscopic examination. Both narrowing and widening, lengthening and shortening can be explained on a passive basis as results of radial and linear tractions, the character and relative degree of which are determined by the magnitude of enlargement of the thoracic cavity during respiration.¹¹ These

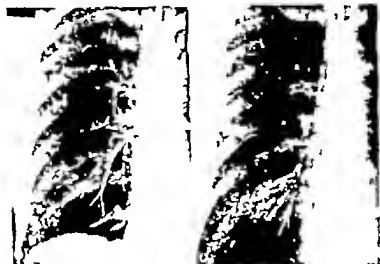
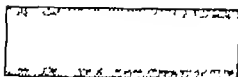


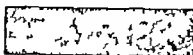
Fig. 237.—Bronchograms made during both phases of the respiratory cycle show changes of length and caliber of the bronchus. a, Expiration; b, Inspiration.

facts are of unusual interest in the correlation of shallow breathing, excessive bronchial secretion and postoperative lobar collapse. In shallow respiration maximal diameter of the bronchi is not obtained. Hilding has shown graphically (Figs. 238 and 239) how relatively small volumes of mucus can bridge a narrowed and shortened bronchus and set up conditions which lead to collapse. That the formation of such diaphragms of secretion is a common natural phenomenon in bronchi when excessive quantities of secretions are present seems likely on the basis of the appearance of bronchograms made during the roentgenologic investigation of many pulmonary problems (Fig. 240).

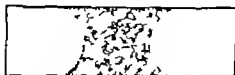
The rate of flow of gas in a tube varies as the fourth power of the diameter of the tube.¹² Hence the accumulation of mucus as a film on



a



b



c

Fig 425.—Hilding: diagrammatic representation of the manner in which an excessive quantity of mucus (stippled) may produce mucous diaphragms, which, acted on by action of cilia, act as piston and participate in the removal of gas from an affected lobule or tube. a, Branches during full inspiration. b, The same branches at full expiration. The formation of mucous diaphragms on inspiration. (Bacteria from Hilding, A. C. Ann. Otol. Rhin. & Laryng. Vol. 24.)

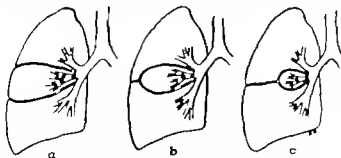


Fig 426.—Hilding: explanation of the events occurring in the development of lobar collapse. a, The occluding mucous mass advances toward the trachea, pro-

the inner surface of a small bronchus reduces its effective diameter disproportionately. This reduction of gas conducting capacity is an additional factor in disturbed ventilation of the corresponding pulmonary segments and therefore in the development of atelectasis.

Efforts to avoid the undesirable effects and sequelae of shallow breathing have been directed toward the several ways in which the depth of respiration can be increased by enlisting the conscious effort of the patient, by the periodic use of a mixture of oxygen with 5 per cent carbon dioxide to bring on hyperpnea, by various rebreathing



Fig. 440—Bronchogram showing the spurring phenomenon by the visceral oil used as contrast medium.

techniques, and by early breathing exercises. Douglas and Haldane showed experimentally that in the hyperpnea of muscular work there was an increase of the depth of breathing with very little change of rate and as a constant accompaniment, a very great increase of the volume of the effective dead space due to dilatation of the bronchi. There is, of course, under such circumstances, a reduction of resistance to the flow of air inward and outward. These are the changes of bronchial and ventilatory function that one seeks to achieve with respiratory exercises, inhalation of carbon dioxide, breathing exercises and other measures.

Another factor which influences the diameter of smaller bronchi and which perhaps is worthy of consideration in clinical practice is the

analgesic used for the patient's comfort. Morphine and other derivatives of opium in effective therapeutic doses, produce bronchial constriction.² The undesirable suppression of the cough reflex by opiates and other analgesics will be discussed in the succeeding paragraphs devoted to the cough mechanism. Whereas morphine is a bronchoconstrictor meperidine hydrochloride (demerol) is a bronchodilator. For that reason it is preferable to use meperidine hydrochloride for the control of pain in the early period after lobectomy. In a further effort to maintain maximal bronchial diameter during the first forty-eight hours after lobectomy the period in which atelectasis was first apparent in the majority of our cases in which lobar collapse developed aminophylline recently has been given intravenously in daily doses of 7½ grains (0.49 gm.).

De Takats and his co-workers ascribed an important role to reflex bronchospasm in the development of postoperative lobular and lobar collapse. No doubt any influence which brings about bronchial narrowing will contribute to the development of pulmonary collapse but experimental and clinical evidence to support the view that bronchospasm reflexly excited by painful stimuli plays a significant role in postoperative lobar collapse is meager.

Since an effective cough is dependent on satisfactory pulmonary ventilation for the necessary air mass, it is with some qualification that one is justified in asserting that an effective cough is the most important single physiologic mechanism in the prevention of collapse. An effective cough is dependent on a large number of factors, some of which, such as pulmonary ventilation and a sensitive cough reflex, have already been considered. Others that should be considered are perhaps more easily expressed in a negative sense that is, by considering those forces which interfere with an effective cough. A priori, any factor which reduces pulmonary ventilation reduces the effectiveness of a cough for example paralysis of the hemidiaphragm, bronchial obstruction of any kind, the presence of large amounts of fluid in the pleural cavity or thickening of the parietal and visceral pleurae. Coryllos mentioned these factors as being concerned with what he called "the inspiratory phase of cough." He described also the compressive and the expulsive phases. In the compressive phase during which a positive pressure is rapidly built up in the lungs behind a closed glottis, he showed that the diaphragm actively contracts to provide a more or less rigid floor. It follows that paralysis of a hemidiaphragm reduces the effectiveness of cough owing to the inability of the hemidiaphragm to participate in the inspiratory or the com-

pressive phase. Furthermore, its paralysis prevents its normal function in the expulsive phase in regulating the expulsion of air. On theoretical grounds, therefore, there are serious objections to phrenectomy during the course of lobectomy. Analysis of our few cases of lobectomy in which interruption of a phrenic nerve was done simultaneously failed to reveal a significantly higher incidence of early postoperative lobar collapse, but it is apparent that the evaluation of one physiologic factor in this complex situation is difficult, to say the least.

Clinically the most obvious factor limiting the effectiveness of the cough is pain. After incision through the thoracic wall even shallow respiration is painful in some degree. Unless steps are taken to relieve it, the pain accompanying the act of coughing is often unbearably severe. Doses of analgesics which will render the patient completely comfortable will reduce to a dangerous degree the sensitiveness of the cough reflex. Therefore, nicety of judgment is required in the administration of analgesics to the patient after lobectomy. The methods that aim toward temporary interruption of the sensory nerve fibers which supply the area of the incision have been mentioned in a previous paragraph.

One other factor for consideration in disturbances of bronchial function is the existence of a bronchopleural fistula. It is chiefly because of the fact that bronchopleural fistulas are present in the first few hours in many cases that a closed drainage or a continuous suction system for the pleural space is provided in all cases. Such small fistulas are particularly likely to exist when the interlobar fissure has been quite incomplete and when a segmental type of resection has been done. These fistulas usually close promptly in the course of a few hours, and are of no serious consequence in the production of early lobar collapse. If, however, the air leak is large and suction sufficient to evacuate this air from the pleural space as rapidly as it escapes from the lung is not maintained, lobar collapse will result immediately.

Small fistulas that exist for only a few hours after lobectomy rarely result in lobar collapse or in the development of empyema. On the other hand, bronchopleural fistulas that develop after some delay as a result of opening of the bronchial stump usually are followed by rapid lobar collapse and empyema. As might be expected on theoretical grounds, bronchoscopic aspiration for the complete removal of excessive bronchial secretions is not sufficient to bring about re-expansion of the lobe under these circumstances. Because the lobe collapses as the result of external pressure and ventilation is no longer possible, secretions do accumulate and they must be removed, but the main

analgesic used for the patient's comfort. Morphine and other derivatives of opium in effective therapeutic doses, produce bronchial constriction.⁹ The undesirable suppression of the cough reflex by opiates and other analgesics will be discussed in the succeeding paragraphs devoted to the cough mechanism. Whereas morphine is a bronchoconstrictor, meperidine hydrochloride (demerol) is a bronchodilator. For that reason it is preferable to use meperidine hydrochloride for the control of pain in the early period after lobectomy. In a further effort to maintain maximal bronchial diameter during the first forty-eight hours after lobectomy, the period in which atelectasis was first apparent in the majority of our cases in which lobar collapse developed, aminophylline recently has been given intravenously in daily doses of 7½ grains (0.49 gm.).

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effort must be directed toward the immediate removal of the air in the pleural space. For this purpose we have preferred a blunt-tipped, large-bore double-curved silver needle that can be inserted through an intercostal space and connected with a motor-driven apparatus that maintains a constant negative pressure of approximately 15 cm. of water. This can be done without moving the patient from his bed. If the lobe can be expanded promptly and completely, closure of the fistula probably can be effected and empyema obviated. There were 11 cases in this series in which there was evidence of early temporary bronchopleural fistula. In 3 cases frank empyema resulted and in an additional 4 the postoperative course was distinguished clinically by prolonged fever.

DISTURBANCES OF RESPIRATORY FUNCTION AFTER LOBECTOMY

Thus far our discussion has been concerned with the disturbances of pulmonary ventilation, bronchial function and cough after lobectomy and the physiologic factors underlying them. These are the disturbances which are responsible for the development of lobar collapse. However, reduction of pulmonary ventilation is associated with commensurate reduction of respiratory gaseous exchange to a degree dependent on the reduction of the volume of functioning alveolar tissue, the pulmonary blood flow, and the reduction of oxygen carrying power of the blood as a result of uncorrected surgical loss of hemoglobin. This disturbance of respiratory function is, after all, the most important disturbance and constitutes the most serious threat to the life of the patient, though it has little to do clinically with the development of lobar collapse. In the uncomplicated case in which lobectomy has been performed, the early postoperative reduction of arterial oxygen saturation, the measure of efficiency of respiratory function, is slight.¹⁰ However, Maier and Courmand have shown that with collapse of the remaining lobe it is commonly severe and prolonged. Oxy-

Recently the nasal catheter has been used instead of the oxygen tent, since the simultaneous use of steam in a croup tent is possible with the former.

COMMENT AND SUMMARY

About a century ago in discussing atelectasis, West wrote: "In considering as a whole the causes which tend to produce bronchial col-

lapse, they seem to resolve themselves into the following. Firstly the existence of mucus in the bronchi which is more liable to produce obstruction according as it is thick and viscid secondly weakness or inefficiency of the inspiratory power however caused thirdly inability to cough and expectorate and thus to remove the obstructing mucus. Of these conditions the first must be considered as the exciting cause, the others as predisposing causes, co-operating with the first, but incapable without it of producing collapse." Subsequent studies have served only to support the accuracy of West's ideas and to analyze the factors which underlie each of these three necessary conditions for the development of lobar collapse and an improvement on his summary of causes from the standpoint of accuracy or succinctness and clarity would be difficult today.

The increase of volume and viscosity of bronchial secretions in most surgical conditions of the lungs is due primarily to infection and inflammation. Bronchosecretory reflexes may play a minor role but the evidence for this is not convincing. A number of measures are of great assistance to the patient in the removal of these secretions from the tracheobronchial tree. By the preoperative use of postural drainage nebulized penicillin solution given intratracheally and penicillin administered intramuscularly one can succeed in reducing the volume and the purulent, viscid character of the sputum in varying degrees. During the course of the operation secretion is removed from the trachea and major bronchi by the anesthetist with catheter aspiration through the intratracheal tube as often as it seems necessary. On completion of the operation bronchoscopy has been performed immediately on most of our patients so that the orifices of the lobar bronchi and their secondary divisions may be visualized and aspirated individually. This may not be necessary in every case, but it seems to add nothing to the risk of the procedure and it enables one to know positively that none of the larger bronchi are filled with secretion. Recently we have been content to depend on thorough tracheobronchial aspiration with a long fiber catheter instead of bronchoscopic aspiration at this stage and there has been no evident increase in the incidence of early lobar collapse.

On the return of the patient to his room he is placed in a bed which has been rigged with a croup tent. Steam in the tent is provided continuously by a kettle. By this means it is hoped that the secretions are made less viscid and therefore easier for the patient to raise by coughing. If even after adequate sedation, the patient's cough is obviously ineffective and rhonchi indicate the presence of excess secre-

tions, vigorous efforts to stimulate the cough are imperative. A small, soft rubber catheter inserted through the nose can usually be made to enter the glottis blindly.¹⁸ Suction applied through this catheter will often remove large quantities of secretion that is brought to the upper part of the trachea by the vigorous cough that results from the stimulus of the catheter in the glottis. Even when the trachea cannot be entered by this method the cough that is evoked by the tip of the catheter touching the structures about the glottis usually will effectively clear the tracheobronchial tree. If these measures fail bronchoscopic aspiration should be done without delay. Particularly during the first forty-eight hours after operation, the period during which lobar collapse is most likely to occur, all possible measures should be taken to prevent atelectasis, for once complete lobar collapse has developed it is commonly necessary to resort to repeated bronchoscopic aspirations before full re-expansion can be effected. Physical signs are difficult to elicit and equally difficult to interpret because of the relative immobility of the patient and the bulky surgical dressing. Changes in the vital signs which so often suggest lobar collapse after an abdominal operation are inconstant and cannot be depended on to indicate the presence of a collapsed lobe after lobectomy. Frequent roentgenograms of the thorax, made with a portable bedside unit, are the only reliable guides to the condition of the lungs in these patients.

There are many factors which contribute to "weakness of respiratory power" as West referred to decreased pulmonary ventilation: injured respiratory muscles; pain on motion of the thoracic wall; limitation of thoracic excursion by the surgical dressing and by the position of the patient in bed; and paralysis of the diaphragm as a result of functional interruption of the phrenic nerve by the surgeon. In order to reduce these disturbances as much as possible, particular attention must be given to the prevention and relief of pain by the care with which the incision is made and closed, by the temporary interruption of the intercostal nerves in the region of the incision and by the po-

caution will favor dependent drainage and prevent elevation of the remaining lobe. Undisturbed diaphragmatic function is necessary for normal pulmonary ventilation; therefore interruption of a phrenic nerve seems undesirable.

The magnitude of change of caliber of the bronchi during respi-

ration is dependent on the magnitude of thoracic excursion. During shallow breathing the bronchi fail to attain their maximal diameter and under these circumstances, are more easily blocked by mucus. The action of cilia and of analgesics which cause bronchiolar spasm has an important bearing on this phase of the bronchial obstruction and lobar collapse. The conscious effort of the patient must be enlisted in attaining good ventilation and the use of demerol and aminophylline probably helps in the avoidance of bronchiolar spasm.

Finally the phases of the cough mechanism have been considered and the factors tending to disturb it in the period after lobectomy have been analyzed. In this consideration the control of pain is particularly important. The co-operation of the patient is essential. Lack of co-operation and small caliber bronchi are most likely responsible for the frequent occurrence of lobar collapse in small children as a complication of lobectomy. The judicious use of sedatives is extremely important, an overdose depressing the cough reflex and an inadequate dose failing to reduce the pain associated with coughing to an intensity that can be readily tolerated.

The presence of a bronchopleural fistula commonly results in rapid lobar collapse and greatly favors the development of empyema. The prevention of bronchopleural fistula is chiefly a technical matter.

Disturbances of intrapulmonary gaseous exchange are not often measurably abnormal after lobectomy. Though when such changes occur they are of major importance to the whole organism, they play no significant role in the pathogenesis of lobar collapse.

That recognition of and attention to the factors contributing to collapse of the remaining lobe or lobes after pulmonary lobectomy have been completely inadequate is attested by the high incidence of this complication in my own experience as well as in that of others.¹⁻³ I believe that conscientious and meticulous efforts to reduce secretion improve ventilation and encourage cough directed along the lines suggested in this presentation will be rewarded by a much lower incidence of early postoperative lobar collapse and therefore of empyema and lobe-destroying chronic pneumonitis.

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THE SURGICAL TREATMENT OF CONGENITAL MEGACOLON*

CLAUDE F. DIXON AND DAVID B. JUDD

Megacolon or Hirschsprung's disease may be defined as a dilatation and hypertrophy of a part or all of the colon in the absence of a gross obstructive lesion. The causative factor is not fully understood at present but there appears to be a congenital imbalance of the innervation of the bowel. As a result, "the nervous mechanism which brings about emptying of the bowel apparently is inferior to that which allows the colon to dilate." With time as a result of marked and persistent dilatation there is great increase in length of the intestine and hypertrophy of the various layers of its walls, particularly the muscularis. There are macroscopic changes also as described by Robertson and Kernohan. They found an atrophy of the ganglia and nerves lying within the wall of the bowel and attributed the loss of function to this deficiency of nerve tissue.

It has been argued that there is inflammation and fibrous tissue in the wall of the bowel and that the atrophy may be due to this; thus, if such is true the atrophy may be an effect, rather than the cause of the disease. However, Robertson and Kernohan found hypertrophy of these same ganglia and nerves in cases of chronic ulcerative colitis, a condition in which there is extensive inflammation and fibrosis throughout the wall of the bowel. They found hypertrophy also in cases of acquired megacolon—that is, megacolon produced by some obstruction such as volvulus. It would seem, therefore, that the improper functioning of the intestine in congenital megacolon is a result of a deficiency of the nervous pathways necessary to initiate and carry out the process of evacuation.

While apparently megacolon or Hirschsprung's disease is a congenital entity it has not been described as a familial or hereditary disease.

Three years ago, one of us (C. F. D.) carried out a subtotal colectomy in

* This case was first carried as an extirpation procedure by means of a long left recto-abdominal type of incision and a three-bladed clamp, forming a

temporary ileosigmoidal stoma. The stoma was closed three months subsequently by anastomosing the ileum with the end of the sigmoid as an intraperitoneal procedure. Recovery followed.

Six years previously the mother of this child had given birth to two boys who died ten days after birth. Autopsies revealed both of these children to have Hirschsprung's disease involving the entire colon. Recently another female child had been born to this mother and had died two weeks later. Autopsy showed a congenital narrowing of the terminal part of the ileum and marked dilatation of the colon.

The rarity of this condition as a possible familial entity makes the above-mentioned instance worthy of mention.

MEDICAL TREATMENT

It is not within the scope of this paper to discuss the various measures used in the medical treatment of this disease. For the most part, the rationale of medical treatment has been an attempt to stimulate the nervous mechanism and incite the bowel to a more nearly normal function. Many drugs have been tried with varying degrees of success. The use of acetyl-beta-methylcholine (methylol) as advocated by Law has attained much favor in recent years. This drug liberates acetylcholine and thus stimulates the parasympathetic ganglia, thereby encouraging peristalsis and evacuation. Klingman recently has reported favorable results from use of the phosphate of 3-diethylamino-2,2-dimethylpropylester of tropic acid (syntropan), a drug which has an atropine-like action. The paradox of similar results from these two pharmacologically opposite drugs serves to emphasize the fact that the fundamental etiology of the condition is not completely understood. It may well be that the degree of success achieved with the various drugs is directly proportional to the amount of attention that is paid to other medical measures in addition, such as use of laxatives, enemas, diet and so forth. It does appear, however, that no matter what medical regimen is carried out, its efficacy gradually diminishes with time so that more radical measures must be employed.

One of the patients in our series was a young boy who was first seen at the age of three years. He was given 40 mg. of methylol daily with very satisfactory response at first. However it soon became necessary to increase the dose and within two years he was taking more than 400 mg. daily but even

ARGUMENTS FOR AND AGAINST SYMPATHECTOMY

Because of the lack of uniformly good results from medical management, it was felt that surgical intervention might achieve a better and more lasting effect. A surgical procedure used extensively in this disease is lumbar sympathectomy. First described by Wade and Royle it has had many advocates since their original report. Penick recently reported apparently satisfactory results with this method of treatment and presented a review of the literature. He concluded that 46 per cent of the patients treated by lumbar sympathectomy had satisfactory bowel function. In 45 per cent more, there was some improvement, and in only 8 per cent was the patient not benefited by the operation. In his series mortality rate in the hospital was 1.6 per cent. He agreed with de Takats that the use of the spinal anesthesia test was of great importance in determining which of the patients might expect a good result from sympathectomy. If evacuation of the bowel is not significantly improved following spinal anesthesia, then a sympathectomy probably will be of little value. Penick advocated a left lumbar sympathectomy as he felt that good results could be obtained with this procedure in the majority of cases and there would be less danger of impotence in the male after this operation than after bilateral sympathectomy. If some improvement was obtained as a result of the unilateral procedure then it could be expected that resection on the right side might enhance the result. If there was no improvement after the first operation he did not feel that more extensive resection would be likely to be of benefit.

There are many arguments against the use of sympathectomy as the treatment of choice for congenital megacolon. If the disease has been present for many months or years, irreversible structural changes are produced in the wall of the bowel which sympathectomy does not remove. Also microscopic changes are present in the ganglia themselves which cannot be corrected by sympathectomy. In the male patient there is danger of impotence particularly if the procedure is carried out bilaterally. Over and above these objections there remains the fact that uniformly satisfactory results in the relief of symptoms are not achieved by the procedure. Many patients who have had sympathectomy have subsequently had part or most of the colon resected before attaining relief.

Crimmon, Vandegrift and Drats, after extensive review of the literature, stated that the ultimate mortality from megacolon treated by medical regimen, with or without sympathectomy, varied with differ

ent authors from 10 to 79 per cent, the average mortality rate being 58 per cent. Most of the patients treated were improved to some extent for a time but the disease progressed and became more difficult to control so that finally more than half of the patients died of the disease. They did not feel that sympathectomy altered this sequence appreciably. In fact they postulated that it might make the condition worse by dulling sensation so that the patient had no warning of impending impaction, perforation or volvulus until too late. Also they felt that the tendency toward volvulus and impaction, and thus perforation was greater after sympathectomy. They advocated subtotal colectomy with establishment of an ileosigmoidal stoma and reported 3 cases in which good results were obtained. In a previous article Crumson and co-workers⁴ reported a series of 24 cases. Twenty of the 24 patients were treated medically of which 6 were having regular bowel movement at the time of the report. Four patients had had sympathectomy and 1 of these was well. In Penick's article his personal series of 11 cases with no deaths was reported. In his classification 7 of the 11 patients had obtained a satisfactory result from sympathectomy. However careful study of his cases reveals that only 3 of the patients were getting along without frequent use of laxatives, enemas or both.

ARGUMENTS FOR AND AGAINST RESECTION

Resection of the diseased segment of bowel has always been considered a good method of treatment for congenital megacolon. It has not been generally used because of the high primary mortality rate and the fear of recurrence of the disease in the remaining portion of bowel. Reference has been made previously to the report by Grumson, Vandegrift and Dratz which presented their results following subtotal colectomy for this disease. They mentioned frequently the danger of recurrence if part of the colon proximal to the diseased segment is left and thus advocated removal of all of the colon above the rectosigmoid. Yeazell and Bell reported 6 cases and no deaths, with satisfactory results in each case. They advocate a two-stage procedure in

— — — — — not delayed, not later a segmental
In 1943 White-
which a resection
had been performed at the Mayo Clinic during the thirty-two year period 1909 through 1940. The report covered 29 cases among which 7 deaths occurred. Of 16 patients on whom reports could be obtained, 13 were having regular bowel movements without the aid of enema or

laxative. Three others were improved but required a laxative frequently and an enema occasionally. Because of the encouraging results presented in this report, it was felt that further study would be of value at this time.

TABLE 1
SURGICAL PROCEDURES EMPLOYED IN 80 CASES OF MEGACOLON

Procedures	Cases
<i>Sympathectomy</i>	
Bilateral lumbar sympathectomy, ganglia 2, 3 and 4	3
Bilateral lumbar and pre-sacral sympathectomy	12
Bilateral resection of splanchnic, celiac and first and second lumbar ganglia	5
Resection of pre-sacral and inferior mesenteric nerves	2
Total, sympathectomy	22
<i>Resection</i>	
Enterostomy, three-bladed clamp	34
Primary anastomosis	10
Winkel's procedure	3
Ileocecectomy with later resection (3 stages)	1
Ileocecectomy with excision of colon	1
Total resection	34

PRESENT STUDY

This study is based on all cases of congenital megacolon in which surgical treatment was given at the Clinic during the thirty-six and a half year period January 1 1909 through June 1945. It embraces a total of 80 cases. Twenty-six patients underwent sympathectomy and 54 underwent resection of part or most of the colon. The 29 cases used in the report made by Whitehouse, Barger and Dixon are incorporated in this study as we have more complete data on many of them. Table 1 shows the various types of procedures performed in this series of 80 cases.

In the group of 28 patients having sympathectomy there were 8 deaths or a mortality rate of 27.7 per cent during hospitalization. One death occurred on the second postoperative day as a result of shock and the other occurred at the completion of an otherwise uneventful operation. One patient has not been heard from since dismissal. Thus, there were 23 cases in which a follow-up could be carried out (Table 8). The 1 patient in whom a good result was obtained was operated on at 17 years of age and still was well and was having regular bowel movements eleven years after operation. The 8 patients mentioned as having fair results were improved by the operation but required and frequently to keep bowel movement regular. One patient was using

TABLE 8
RESULTS FOLLOWING SYMPATHECTOMY FOR MEGACOLON

Procedure	Patients Traced	Results		
		Good	Fair	No Improvement
Bilateral lumbar sympathectomy	8	0	8	0
Bilateral lumbar and presacral sympathectomy	10	0	4	6
Bilateral resection of splanchnic, celiac, and first and second lumbar ganglia	6	0	0	6
Resection of presacral and inferior mesenteric nerves	4	1	1	2
Total	28	1	13	14

mineral oil daily. Six others were resorting to enemas at least every two days and that they had not been able to have regular bowel movements were

In the 54 cases in which resection was carried out, there were 9 deaths or a mortality rate of 16.7 per cent during hospitalization. In this regard it is interesting to note the mortality statistics in relation to the various stages of the hospital care associated with colonic surgery. In the period from 1909 through 1919 the hospital mortality

rate was 50 per cent. During this period preoperative and postoperative care was at a minimum. In the period from 1920 through 1940 the mortality rate dropped to 17.4 per cent. During that time preoperative preparation became established as a routine. Laxatives, colonic irrigations and nonresidue diets were used to clean out the bowel. Supportive measures such as parenteral administration of fluids, vitamins, plasma and blood were employed freely as indicated. During the early part of this period intraperitoneal administration of vaccine became established as a definite ally to immune infection. In the later years this adjunct has been succeeded by the sulfonamides which are more easily administered, are less likely to cause discomfort or serious reaction and appear to be more efficacious in reducing the incidence of infection. Since publication of the previous report, which covered the period 1941 through June, 1943, there have been 25 additional cases of congenital megacolon in which resection of the diseased bowel was performed with 1 death or a mortality rate of 4 per cent during hospitalization. This steady and marked improvement in mortality rate is due, we believe, more to adequate preoperative preparation of the patient than any refinement in surgical technique. It has been achieved by close co-operation between internist, pediatrician and surgeon, and credit is due as much to the first two as to the last. We believe that with continued co-operation of this character these results may be improved still further so that the risk of the operation will not be a contraindication to its use as the procedure of choice in the therapy of this disease.

Another factor of great importance when operative mortality is considered is the patient's age. It has been emphasized frequently that patients under 3 years of age do not stand abdominal operations well, particularly when resection of the bowel is performed. Of the 9

death in the series of —
or you
were

In other words, for children 3 years of age or younger the mortality rate was nearly 45 per cent. In comparison with this, there were 15 patients from 3 to 10 years of age among whom there were 2 deaths or a mortality rate of less than 16 per cent during hospitalization. The other 3 deaths in the series of 54 cases were of patients 12, 31 and 55 years of age respectively. Thus, if operation is avoided in the very young infants, the procedure may be performed at much less risk.

The 1 death in the recent series of 25 cases was that of a boy 3 years of age who had tremendous dilatation and hypertrophy of the entire colon and

In the group of 23 patients having sympathectomy there were 2 deaths or a mortality rate of 7.7 per cent during hospitalization. One death occurred on the second postoperative day as a result of shock and the other occurred at the completion of an otherwise uneventful operation. One patient has not been heard from since dismissal. Thus, there were 22 cases in which a follow-up could be carried out (Table 2). The 1 patient in whom a good result was obtained was operated on at 17 years of age and still was well and was having regular bowel movements eleven years after operation. The 8 patients mentioned as having fair results were improved by the operation but required aid frequently to keep bowel movements regular. One patient was using

TABLE 2
RESULTS FOLLOWING BOWEL RESECTION FOR MECONIUM

Procedure	Patients Treated	Results		
		Good	Fair	No Im- provement
Bilateral lumbar sympathectomy	2	0	3	2
Bilateral lumbar and presacral neurectomy	10	0	4	6
Bilateral resection of splanchnic, colic and first and second lumbar ganglia	0	0	0	0
Resection of presacral and inferior mesenteric nerves	2	1	1	0
Total	22	1	8	14

mineral oil daily. Six others were resorting to enemas at least every third day in addition to the use of mineral oil. One patient stated that operation improved his condition but that he continued to have

deaths or a mortality rate of 16.7 per cent during hospitalization. In this regard it is interesting to note the mortality statistics in relation to the various stages of the hospital care associated with colonic surgery. In the period from 1900 through 1919 the hospital mortality

the group of 54 cases. After deletion of the 9 deaths and the 2 patients who had not been heard from since dismissal there were 43 patients on whom follow-up data were available. Thirty-six of these patients were having regular bowel movements without the aid of laxatives or enemas. There were 6 cases in which there was definite improvement after operation but the bowels were not moving regularly. 2 of these patients were regulating elimination by the daily use of mineral oil and 2 others were employing an enema occasionally. One of these 6 patients a 6 year old boy often did not have a bowel movement in two or three days his mother thought that he was lazy and did not try to

TABLE 3

RESULTS FOLLOWING RESECTION OF THE BOWEL FOR MEGACOLON

Procedure	Patients Traced	Results		
		Good	Fair	No Improvement
Enterostomy	27	21	6	0
Primary anastomosis	6	7	0	1
Milestones	6	6	0	0
Proctostomy and subsequent resection in three stages	1	1	0	0
Proctostomy and exclusion of colon	1	1	0	0
Total	45	36	6	1

obtain elimination at regular intervals. Another of the 6 patients still had cramps and occasionally some distention but was much better than before surgical intervention. His local physician suspected that there was a constriction at the site of the anastomosis. Unfortunately he did not return so that we did not have an opportunity to make a first hand examination. One patient wrote that she was no better after operation than before. Two years after operation she continued to have much the same symptoms as she had had previous to surgical treatment. She too, did not return for an examination.

This is a small series of cases upon which to base any conclusion. However according to our experience with treatment of megacolon 87 per cent of the patients who underwent resection of the diseased

the rectum. A subtotal colectomy was performed and the divided ends of ileum and rectosigmoid were brought out through the abdominal wall in three-bladed clamp, thus establishing a double-barreled sigmoidal stoma. The patient progressed well after this procedure but since his mother had difficulty in controlling the fecal discharges, it was decided to close the artificial stoma sooner than originally was intended. After the closure, it soon became evident that the bowel was not functioning properly. In spite of having from one to three loose stools daily, the patient became markedly distended and had much crampy abdominal pain, nausea and vomiting. A nasal tube was passed into his stomach and continuous suction was applied. Although much fluid and gas were removed in this manner, he continued to vomit, the material coming out around the tube. A Witzel type of ileal stoma was established, which apparently did relieve the nausea and vomiting, but the abdominal distention and crampy pain persisted. During all of this time the patient continued to have daily movements through the rectum. Because of the profuse discharge from the ileal stoma an attempt was made to improve nutrition by means of a continuous drip of a high protein formula by way of a nasointestinal tube introduced into the stomach. After two weeks on this regimen it appeared that bowel function was improving, but a fulminating tracheobronchitis developed and, regardless of the tracheostomy, the patient died 116 days after the closure of the ileosigmoidal stoma. Permission for necropsy was not obtained but it was the clinical impression that there was more of a functional imbalance in bowel function than a mechanical obstruction.

Among the 20 cases in the report made by Whitehouse, Bergen and Dixon there was 1 patient who was well after resection of the sigmoid and establishment of a double-barreled colic stoma. Closure of the colic stoma was carried out after that report had been made but the patient succumbed from peritonitis on the seventh postoperative day. In the group of 20 cases there were 9 deaths in the hospital. Four of these deaths were due to peritonitis, 2 of which followed closure of a previously established colic stoma. One death, and possibly a second as described above, was due to intestinal obstruction. One patient died of pneumonia, 1 of postoperative shock and 1 on the seventh postoperative day of scarlet fever which appeared on the fifth postoperative day.

The types of procedures employed in the group of 54 cases are presented in Table I. Interestingly enough, the mortality rate during

the 3 patients undergoing the Mikulicz operation (1941) (1942) (1943) (1944)
Table 3 shows the results in relation to the various procedures in

frequently it was demonstrated that part of the proximal segment
 2. — — — — — which studies had revealed it

been anticipated. The numbers in Table 4 that represent the frequency of involvement of the transverse segment of colon include all cases in which any of this segment was involved. In the majority of these cases less than half of the transverse colon was involved. Usually the transverse colon constituted the upper limit of the involvement in the splenic flexure and descending colon.

Usually the procedure of resection is considered the last resort in the management of this disease. In our group of 54 cases there were 21 in which some form of therapy had been given previously. Five

TABLE 4
 PERCENT OF COLON INVOLVED IN 60 CASES OF MEGACOLON

Procedure	Cases	Part of Colon Involved				
		Sigmoid	Descending	Transverse	Ascending	Entire
Resection	21	48	41	27	10	9
Sympathectomy	24	20	29	18	8	8
Total	45	68	70	45	18	17

patients had used mecholyl, 2 of whom had obtained temporary relief. Two patients had tried neostigmine (prosthigmine) and 2 had tried diathermy, all without benefit. Syntropan had been employed in 2 patients, 1 of whom had had temporary relief when this drug was combined with kondrenul. In 1 case roentgen treatment had no effect. Four patients had undergone sympathectomy previously without benefit. In 4 cases colostomy had been performed; in 2 of these, the colic stoma was later closed but recurrence of symptoms followed.

SUMMARY AND CONCLUSIONS

Congenital megacolon or Hirschsprung's disease ensues from an imbalance in the nervous mechanism which controls the function of the bowel. As a result the bowel tends to dilate more readily than to contract. This imbalance in turn may be due to a deficiency of ganglia and fibers in Auerbach's plexus. As a result of prolonged and marked

bowel were completely relieved of their symptoms and an additional 11 per cent were definitely improved. Of the 43 traced patients who survived resection 89 per cent were improved and 84 per cent were completely relieved of symptoms. This is in contrast to our results for sympathectomy in this disease. Of the 23 patients who survived sympathectomy and who were traced, 14 or 61 per cent were not benefited by surgical treatment. These statistics are based on a follow-up period, in each case, at a minimum of one year after operation with 5 exceptions. These 5 patients were well but they had been operated on so recently that the follow-up could cover only three, four and five months respectively. The majority of the 23 patients in this group had undergone operation two or more years previous to the time they made the report. None of the patients experienced temporary relief after resection and then later had a recurrence of symptoms referable to megacolon. On the contrary some patient continued to have mild symptoms for a time after operation but eventually recovered completely without further treatment.

Our experience does not substantiate the often expressed fear that the disease will recur in the remaining part of the colon if only a partial colectomy is performed. Of the 54 cases in which resection was performed there were 41 in which half or less than half of the colon was removed. Twenty five of these 41 patients had complete relief of symptoms, and in 18 of the 23 only the sigmoid or sigmoid and descending colon had been removed from five to twenty-one years previously. It was not possible to make postoperative roentgenologic examinations of the remaining part of the colon in all cases; thus we do not have complete information as to the postoperative condition of the bowel. Dilatation of the colon was demonstrated in 5 cases in which such examination was carried out but 2 of these patients continued to have normal bowel function four years after examination. It may be that demonstrable dilatation of the colon is present postoperatively in some cases but apparently this does not interfere with normal function.

The extent of the resection performed in each case in this series was determined primarily by the amount of bowel involved at the time of operation. Table 4 shows the frequency of involvement of the various segments of bowel. The disease occurred predominantly in the left portion of colon particularly the sigmoid. This segment was not invariably involved, however, as there were 11 cases in which the right half of the colon was diseased while the descending colon and sigmoid were normal. The amount of the colon affected by the disease was determined at operation after thorough cleansing of the colon.

symptoms, particularly the symptoms of abdominal distention which when marked often causes the costal margins to flare out. Also it appears that if the symptoms are not well controlled by medical measures the danger of ultimate disaster is great unless more effective measures are employed.

The fear that the disease will recur in the remaining portion of bowel after partial colectomy is not substantiated by our experience with this procedure. In the group of 54 cases in which resection was performed, there were 41 in which half or less than half of the colon was removed and in no case do we have evidence of recurrence of the disease in the remaining portion of the colon. In 25 of these 41 cases there was complete relief from symptoms.

For these reasons we believe that in cases of congenital megacolon the treatment of choice is resection of the diseased segment of bowel. If the patient is 3 years of age or younger surgical treatment should be delayed and the symptoms should be controlled as much as possible by medical measures until the child becomes older. It is our belief however that in the majority of cases resection of the diseased bowel will need to be performed before complete relief from symptoms is obtained.

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dilatation the bowel becomes elongated and its walls hypertrophied. Attempts to overcome the imbalance by drug therapy and other medical measures have met with variable and incomplete success. Resection of the lumbar sympathetic ganglia and nerves is a surgical means of attacking the problem from the same angle and it too has achieved uncertain results. Many authors have expressed satisfaction with this method of treatment but our experience has not been encouraging. Of 20 patients in whom sympathectomy was performed, only 1 appeared to have a satisfactory result. Aside from this, there remains the fact that sympathectomy does not remove the pathologic condition present and it appears that the danger of disaster such as from obstruction, volvulus or perforation of the diseased segment of bowel is not lessened by sympathectomy.

On the other hand, our experience with resection of the diseased bowel has been most encouraging. Of all the patients in whom resection was performed 78 per cent were improved and 67 per cent were completely relieved of their symptoms. If only traced patients are considered 98 per cent were improved and 84 per cent were completely relieved. The two main reasons that resection has not been in greater favor as the treatment of choice for congenital megacolon are, first, a high primary mortality rate and second, fear of recurrence in the portion of colon not removed. It is our belief that the mortality rate during hospitalization need not be high following this procedure. With proper co-operation between pediatrician, internist and surgeon, all facilities for preoperative preparation of the patient can be utilized to the fullest extent and the risk of the operation can be reduced accordingly. In our most recent series of cases the mortality rate during hospitalization was 4 per cent, and we feel that the rate will be even lower in the future.

Resection should not be performed in children under 3 years of age unless absolutely necessary since they do not tolerate resection of the bowel well. The postoperative mortality rate in this age group was nearly 45 per cent. In the majority of such cases the symptoms can be controlled reasonably well for a time by medical measures, including diet, laxatives, enemas and drugs such as mechloryl; therefore these young children should be carried along on the regimen until they are 3 years of age or older. However, it is not advisable to prolong the regimen to the presence of persistent and severe symptoms such as constipation, abdominal distention, nausea and vomiting. Frequently by the time the child is of school age, it becomes apparent that he is not like "normal" youngsters and the parents as well as the patient want something done to achieve more nearly complete relief from the

JEJUNO-ILEAC INSUFFICIENCY ITS RELATION TO THE SPRUE SYNDROME

E. LEONARD POSEY JR. AND J. ARNOLD BARGEN

THE pathologic condition which has been recognized as a deficiency state akin to or representative of the sprue syndrome is due to various causes (Table 1). In some of the reported cases of the sprue syndrome in which the patients have had symptoms of a deficiency state exploratory laparotomy or necropsy has disclosed an unsuspected disease of the small intestine or has revealed that a variable portion of the small intestine previously had been isolated by a short-circuiting procedure.

Bennett and Hardwick noted that the syndrome of steatorrhea, tetany and macrocytic anemia may be encountered in cases of malignant and excruciating disease of the small intestine, in cases of gastrocolic fistula, and in some cases of *tuberculosis mesenterica*. They considered deficient absorption from the small intestine to be the primary cause of the difficulty in these instances. They proposed that, analogous to renal insufficiency, this syndrome be termed "jejuno-ileal insufficiency."

Manson Bahr offered a further commentary on the condition in 1941. He postulated that sprue is the expression of an inefficient functioning of the small intestine. He said that in the sprue syndrome the essential etiologic factor is situated in the intestinal tract and is of such a nature and extent as to interfere with the absorption of one or several vitamins necessary for life.

In this consideration we wish to re-emphasize that sprue is a syndrome which may have a diverse origin (Table 1).

It becomes obvious that (1) an intact wall of the small intestine, (2) a normally functioning mucosa, (3) normal peristalsis and normal transportation of the chyme, (4) the presence of adequate digestive enzymes and bil., and (5) intact lymphatics are essential for adequate digestion and absorption. A break in any of these may eventuate in a deficiency state. Impairment of the absorptive ability of the small intestine, almost universally mentioned as the underlying cause of jejuno-ileac insufficiency " " " " " One of the cases reported by Brock bears out this hypothesis. In this case macrocytic hyperchromic anemia developed in the course of a stricture of the small bowel. Oral administration of adequate doses of liver extract did not produce any

TABLE I
CAUSES OF JEJUNO-ILEAL I SUFFICIENCY

- I Diseases of the small intestine
 - 1 Regional enteritis, including sarcoidosis
 - 2 Amyloidosis
- II Diseases of segments of small and large intestine
 - 1 Regional enterocolitis
 - 2 Ulcerative tuberculosis
 - 3 Chronic relapsing dysentery
 - 4 Strictures
 - a Peridiverticulitic
 - b Secondary to tuberculosis
 - c Secondary to regional enteritis
 - d Congenital
 - e Neoplastic (unknown origin)
 - f Extrinsic
 - 5 Neoplasms
 - a Benign
 - b Malignant
 - 6 Lymphogranulomatosis (Whipple disease)
 - 7 Generalized polyps of the intestine
 - 8 Congenital malrotation of the intestine
- III Short-circuiting of the intestine
 - 1 Complicating suppurative disease of the abdomen
 - 2 Complicating malignant disease
 - 3 Complicating regional enteritis
 - 4 Short-circuiting of intestine
 - a Resection of small intestine
 - b Gastrojejunocolic fistula
 - Partial gastrectomy followed by gastrojejunostomy (Pol)
 - c Surgical error
 - (1) Gastrojejunostomy
 - (2) Gastrocolostomy
- IV Parasit infestation
 - 1 Giardia lamblia
 - 2 Diphylobothrium latum
 - 3 Balantidium coli
- V True deficiency diseases
 - 1 Sprue (tropical and nontropical) and idiopathic steatorrhea
 - 2 Pellagra
 - 3 Pernicious anemia
- VI Diseases involving the mesenteric lymph nodes
 - 1 Lymphoblastoma
 - 2 Metastatic carcinoma
 - 3 Tuberculosis (tuberculous enteritis)
 - 4 Lymphogranulomatosis (Whipple disease)
 - 5 Parasitic involvement
 - a Filariasis
- VII Metabolic disorders
 - 1 Diabetes and diarrhea
 - 2 Addison disease
 - 3 Exocrine disease
 - 4 Hyperthyroidism

sidered the result of defective absorption or excessive loss of the erythrocyte-maturation factor.^{2, 7, 8, 21, 22} The gastric achlorhydria which is a common accompaniment is felt to play an etiologic role in certain cases.¹⁴ Hawkey and Meulengracht reported a case in which intestinal stricture was associated with pernicious anemia and they viewed 25 similar cases that had been reported in the literature. Free hydrochloric acid was known to have been present in the gastric juice in 3 of these cases and achlorhydria was known to have been present in 18 cases. In 1 of the cases in which free hydrochloric acid was present, Castle's intrinsic factor also was present. Butt and Watkins expressed the opinion that a defective utilization of the erythrocyte-maturation factor might be important, while Barker and Hummel said that the absorption of hemotonic substances from the diseased small bowel might be significant. It is interesting to note that in some cases in which megaloblastic anemia is associated with jejuno-ileal insufficiency the anemia will not respond to the administration of liver extract but will disappear promptly after surgical correction of an abnormality.^{7, 14, 23}

The clinical picture may become still more complicated by the appearance of a macrocytic hypochromic anemia,⁶ the result of severe combined deficiencies of iron and the erythrocyte-maturation factor. Such a clinical picture also has been observed in the course of non-tropical sprue.⁸

RESECTION OF THE SMALL INTESTINE

The amount of small intestine that can be removed without interfering seriously with the bodily economy of human beings varies

out affecting the digestive functions seriously.^{2, 3, 8, 13, 24} Cases 1 to 6 included in this paper suggest the importance of the personal factor in evaluating observations along these lines.

STRUCTURES OF THE SMALL INTESTINE

Review of this subject have been made by various authors, including Hawkey and Meulengracht, Butt and Watkins and Barker and Hummel who found various types of deficiency disease associated with enteric strictures. Bennett and Hardwick also have commented on this association. The stricture may be of unknown origin, second

posite picture would appear to be an uncommon and rather extreme finding.

Table 2 shows the more important dietetic elements that may be lost and the effects that their loss may produce.

The different types of anemia that may be associated with jejunoileal insufficiency are of particular interest. The loss of iron naturally produces microcytic hypochromic anemia. This commonly occurs in

TABLE 2
RESULTS OF LOSS OF ESSENTIAL CRITICALS IN FOODS

Chemicals and Foods	Results of Loss
Fat	Fatty stools, loss of weight, loss of calcium (as soap), decreased concentration of fat in blood
Protein	Constipation, negative nitrogen balance, hypoproteinemias, loss of weight, edema
Carbohydrate	Fermentation of stools, abdominal distention and flatulence, fat glucose tolerance curve, decreased concentration of blood sugar
Vitamin A	Night blindness, xerophthalmia, keratinosis, bronchitis
Vitamin B	Glossitis, cheilosis, angular stomatitis, dermatitis, peripheral neuritis, diarrhea, pellagra, dermatitis, hypochromic anemia
Vitamin C	Gingivitis, bleeding tendency, scurvy
Vitamin K	Hypoprothrombinemia, bleeding tendency
Iron	Hypochromic microcytic anemia
Calcium	Hypocalcemia, tetany, rickets, deformed bones, osteoporosis

the early stages of the syndrome. This anemia may be further aggravated by a deficiency of members of the vitamin B complex, as well as by bleeding produced by the hypoprothrombinemia secondary to vitamin K deficiency and by a decrease in the amount of vitamin C stored in the body.

The appearance of megaloblastic anemia marks a more advanced stage of the inefficiency. This condition which cannot be distinguished hematologically from pernicious anemia¹² is usually con-

ary to tuberculosis of the small bowel ² postanastomotic,¹ or it may complicate regional enteritis.⁷ It also may be extreme, as it was in case 5.

Stenosis of the small intestine usually is silent but symptoms of intestinal obstruction may occur if the lumen of the intestine becomes so narrow that the passage of chyme is impeded. Since the contents of the small intestine are liquid, symptoms do not occur unless a considerable degree of narrowing is present. Indeed, Paul has said that the lumen of the small intestine may be reduced to the diameter of a lead pencil without producing symptoms. Severe deficiency disease, however, may develop in association with lesser degrees of stenosis. Brook reported a case in which multiple strictures had reduced the diameter of the small intestine to $\frac{3}{8}$ inch (1.27 cm.) in some places. Hawley and Meulengracht reported a case in which multiple strictures had reduced the diameter of the small intestine to 2 to 4 cm. at ten places.

Various manifestations of insufficiency of the small intestine have been observed in cases of intestinal structure. These include anemia of various types,^{1, 2, 3} steatorrhea,^{1, 2, 3} impaired absorption of dextrose,¹ defective absorption of vitamin C,⁴ achlorhydria, absence of Castle intrinsic factor,⁵ osteoporosis, glossitis and pellagra dermatitis.

INTESTINAL SHORT-CIRCUITING

Gastrojejunocolic fistula: frequently associated with deficiency disease. Fairley and Halper reported 3 cases in which the symptoms closely resembled those of sprue. Bennett and Hardwick said that gastrojejunocolic fistula provides conclusive evidence that jejunoileal insufficiency is the cause of symptomatic sprue, since the entire small intestine is short-circuited by the fistula and thus, for practical purposes, is functionless. Deficiency states including steatorrhea, macrocytic hyperchromic anemia, various types of vitamin deficiency and calcium depletion have been observed in cases of gastro-ileal fistula, duodenocolic fistula, and intestino-intestinal fistula. In cases in which these lesions have been present as much as 93 per cent of the stools have consisted of fat.¹⁰

DISEASES OF THE WALL OF THE SMALL INTESTINE

Various diseases of the small intestine at times have produced symptoms which have simulated those of symptomatic sprue. Tuberculosis,

September 1946 At that time, physical examination disclosed paller and pitting edema of the ankles The erythrocyte count was 3,40,000 and the value for the hemoglobin was 10.8 gm per 100 cc of blood The value for the serum protein was 4.0 gm per 100 cc and the albumin-globulin ratio of the serum was 1.02:1 Roentgenologic examination of the colon was performed on September 23 At that time, the pattern of the mucous membrane of the colon suggested the presence of a deficiency state (Fig 241a) The patient returned to his home on September 24, 1946 A high caloric diet was prescribed and the patient was advised to take vitamins, iron and folic acid

The patient returned to the Clinic on April 28, 1947 The anemia had persisted and he had received forty transfusions of blood since his last visit to the Clinic Although he had been on a diet which furnished 4,000 to 5,000 calories, he had not gained any weight He was passing 2 or 3 loose stools daily Undigested food occasionally had been passed from the rectum one hour after it had been eaten His stools occasionally had contained a small amount of blood Moderately severe edema of the feet had occurred at times when hematologic examination had disclosed that the anemia was most severe The edema had been associated with listlessness, weakness and anorexia

The patient was hospitalized for further study He weighed 90½ pounds (41 kg) at this time Although he was emaciated, he was not having any distress The results of physical examination were not significant The erythrocyte count was 4,410,000 and the leukocyte count was 7,600, but the patient had received a transfusion of blood just before he returned to the Clinic The value for the hemoglobin was 18.0 gm per 100 cc of blood On several occasions, examination of a blood smear disclosed that some of the erythrocytes had a tendency to be abnormally large (macrocythemia) The value for the blood urea was 32 mg per 100 cc The value for the serum protein was 4.5 gm per 100 cc and the albumin-globulin ratio was 1.5:1 The concentration of serum calcium was 8.6 mg per 100 cc The values for the cholesterol, fatty acids and total lipids were 80 mg, 164 mg and 244 mg per 100 cc of plasma, respectively The sedimentation rate of the erythrocytes was 8 mm in one hour (Wintrobe ———) in twenty-four hours (normal is 15 to 18 mm)

chloric acid in the gastric contents after histamine had been administered Five of the patient's stools were examined for blood while he was in the hospital The benzidine test disclosed blood in all five instances and the guaiac test indicated that blood was present in three of the stools On May 27, 1947, examination revealed that 66 per cent of the stools by dry weight consisted of fat The roentgenoscopic appearance of the colon was the same as it had been at the time of the patient's previous visit to the Clinic The appearance of the mucosa in the small intestine was suggestive of a deficiency state (Fig 241b)

The patient received a high caloric, high protein, low fat diet which was supplemented with vitamins Liver extract, folic acid and iron were administered orally and protein hydrolyzate was administered by enema

colon did not disclose any abnormality. While the patient was receiving approximately 100 gm. of fat daily it was found that 36 per cent of the stools by dry weight consisted of fat. A subsequent determination disclosed that the stools contained 16.9 per cent of fat. The diagnosis at that time was steatorrhea secondary to resection of a portion of the small intestine. The patient was discharged on February 27, 1946.

The patient returned to the Clinic on December 10, 1947, because he had continued to have intermittent attacks of diarrhea and steatorrhea. The attacks had lasted for from one to two weeks. After the termination of each attack, he had not had any symptoms for several days. Physical examination did not disclose any abnormality. Metabolic studies revealed that the patient lost an average of 2.9 gm. of nitrogen and 34.6 gm. of fat daily while he was receiving approximately 100 gm. of fat and 120 gm. of protein daily. He was advised to take 925 grains (15 gm.) of pancreatin daily in the form of enteric-coated tablet. He also was advised to increase his intake of food and to regulate his activities. The patient was discharged on January 6, 1948. He has gained weight since he left the Clinic but he still is having an occasional attack of diarrhea.

In this case the deficiency caused diarrhea, steatorrhea and cretazorrhea. The patient lost an average of 2.9 gm. of nitrogen daily while he was receiving approximately 120 gm. of protein. There was a slight reduction in the value for the serum calcium and in the values for the cholesterol and cholesterol esters in the plasma. The steatorrhea alone accounted for a loss of 480 calories daily. There also was some irregularity in the absorption of fat. On one occasion the amount of fat in the stools was found to be normal.

CASE 2.—A laborer, aged 30 years, first came to the Clinic on May 14, 1944, because of abdominal cramping, diarrhea, rectal bleeding and loss of weight. These symptoms had developed suddenly about six years before he came to the Clinic. Roentgenographic examination of the small intestine revealed changes that were typical of regional enteritis. A laparotomy disclosed subacute inflammation of the terminal 3 to 4 feet (91 to 124 cm.) of the ileum. A portion of the intestine which included 60 cm. of the terminal portion of the ileum, the cecum, the appendix and 20 cm. of the ascending colon was removed, and side-to-side ileocolostomy was performed. Pathologic examination revealed subacute and chronic regional enteritis which involved chiefly the

home on June

The patient apparently improved for several weeks after he returned to his home. Severe anemia then developed and repeated transfusions of blood became necessary. The number of stools increased gradually until the patient was having 5 or 6 bowel movements per day. He returned to the Clinic in

dence of a deficiency state: hypocalcemia, a decrease in the concentration of plasma lipids, and by hypoproteinememia, achlorhydria, hypoproteinememia and edema. The anemia is of the hypochromic type. Since repeated examination of blood smears discloses that there is a tendency for some of the erythrocytes to be larger than normal, the anemia can conceivably be classified as macrocytic hypochromic anemia. The anemia in this case was attributable to the following causes: (1) deficient absorption of iron, (2) achlorhydria, (3) hypoproteinememia and chronic bleeding from the intestine and (4) deficient absorption of the erythrocyte-maturation factor.

CASE 3—A girl, aged 14 years, came to the Clinic on July 6, 1943, because of bloody stools and cramp in the upper part of the abdomen. A diagnosis of regional jejunitis was made on the basis of the roentgenologic findings. A high caloric, low residue, bland diet was prescribed and succinylsulfathiazole and codene were administered. The patient was dismissed from the Clinic on July 14. She was instructed to continue the treatment at her home. Her physical condition was satisfactory until March, 1946, when her former symptoms returned after an attack of ptomaine poisoning, which had occurred while she had been in Mexico on her honeymoon.

In August, 1946, the patient returned to the Clinic because of nausea and abdominal cramp. The diseased segment of the jejunum was excised and the continuity of the jejunum was re-established by an end-to-side jejunojunction. The excised segment of the jejunum was 104 cm. long. The pathologist made a diagnosis of subacute regional enteritis. In the central 25 cm. of the excised segment, the involvement was continuous. Throughout the remaining portion of the excised segment, there were scattered lesions which were somewhat annular in shape. Macroscopic examination revealed lesions which resembled the lesions of sarcoidosis. The patient was dismissed from the Clinic on October 5, 1946.

The patient continued to improve until January, 1947, when the number of stools began to increase gradually. The stools were light colored, foamy

symptoms of vitamin deficiency. The results of physical examination were not significant. The erythrocyte count was 4,450,000 and the leukocyte count was 7,300. The value for the hemoglobin was 12.3 gm. per 100 cc. of blood. Examination of a blood smear revealed that some of the neutrophils contained deeply staining, basophilic granules ("toxic granules"). Hematologic examination also revealed that 0.4 per cent of the erythrocytes were reticulated. The sedimentation rate of the erythrocytes was 37 mm. in one hour. The value for the serum calcium was 9.3 mg. per 100 cc. The Exton-Hose test disclosed that the patient's tolerance for dextrose was slightly decreased. Examination of

Twenty-five milligrams of testosterone propionate was administered subcutaneously on four occasions. The patient gradually gained strength and the number of stools decreased until he was having only 1 or 2 bowel movements each day. His weight increased to 93½ pounds (42.8 kg). There was a steady deterioration of the hematologic picture. On May 20, sternal aspiration revealed a normoblastic type of marrow and some evidence of left shift in both the erythrobl and myeloid line. On May 26, the erythrocyts and leukocyts

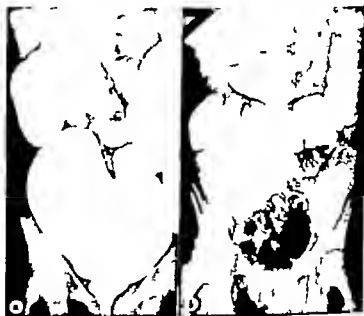


Fig. 811—*a*, Roentgenogram of the colon in case 2, showing changes suggestive of deficiency state; *b*, Roentgenogram of the small intestine in case 2, showing changes suggestive of deficiency state.

counts were 3,200,000 and 5,600 per cubic millimeter of blood, respectively.

In case 2, the resection of the terminal portion of the ileum led to the development of a deficiency state in a relatively short time. Jejunale ileal insufficiency is evidenced by steatorrhea, mentigenologic cri-

dence of a deficiency state, hypocalcemia a decrease in the concentration of plasma lipids, and by hypoproteinememia achlorhydria, hypoproteinemia and edema. The anemia is of the hypochromic type. Since repeated examination of blood smears discloses that there is a tendency for some of the erythrocytes to be larger than normal the anemia can conceivably be classified as macrocytic hypochromic anemia. The anemia in this case was attributable to the following causes: (1) deficient absorption of iron, (2) achlorhydria, (3) hypoproteinememia and chronic bleeding from the intestine and (4) deficient absorption of the erythrocyte-maturation factor.

CASE 3—A girl, aged 14 years, came to the Clinic on July 6, 1943, because of bloody stools and cramp in the upper part of the abdomen. A diagnosis of regional jejunitis was made on the basis of the roentgenologic findings. A high caloric, low residue, bland diet was prescribed and succinylsulfathiazole and codrene were administered. The patient was dismissed from the Clinic on July 14. She was instructed to continue the treatment at her home. Her physical condition was satisfactory until March, 1946, when her former symptoms recurred after an attack of ptomaine poisoning, which had occurred while she had been in Mexico on her honeymoon.

In August, 1946, the patient returned to the Clinic because of nausea and abdominal cramp. The diseased segment of the jejunum was excised and the continuity of the jejunum was re-established by an end-to-side jejunojejunostomy. The excised segment of the jejunum was 103 cm. long. The pathologist made a diagnosis of subacute regional enteritis. In the central 25 cm. of the excised segment the pathological changes were as follows:

what a
resembled the lesions of sarcoidosis. The patient was dismissed from the Clinic on October 8, 1946.

The patient continued to improve until January 1947 when the number of stools began to increase gradually. The stools were light colored, foamy

examination of a blood smear revealed that some of the neutrophils contained deeply staining, basophilic granules ("toxic granules"). Hematologic examination also revealed that 0.4 per cent of the erythrocytes were reticulated. The sedimentation rate of the erythrocytes was 37 mm. in one hour. The value for the serum calcium was 9.3 mg. per 100 cc. The Exton-Bow test disclosed that the patient's tolerance for dextrose was slightly decreased. Examination of

was 0.8 mg. per 100 cc. and that for the serum phosphorus was 3.3 mg. per 100 cc. The result of a glucose tolerance test was normal. The patient excreted 3.3 mg. of 17-ketosteroids in twenty-four hours. Analysis of the gastric contents by the method of Topfer revealed that the value for the free hydrochloric acid was 36 and the value for the total acidity was 82.

Röntgenologic examination of the rectum and sigmoid disclosed extensive chronic ulcerative colitis. The suspension of barium could not be forced higher than the sigmoid owing to the presence of extreme tenderness. Roentgenologic examination of the small intestine did not disclose any abnormality. There was no evidence of a stricture at the site of the ileocolic anastomosis. Proctoscopic examination revealed changes that were typical of the streptococcal type of chronic ulcerative colitis. The results of macroscopic and bacteriologic examination of the stools were not significant. Fat accounted for 88.7 per cent of the dry weight of the stools.

The patient received a high caloric, high protein diet which contained minimal amount of fat. The diet was supplemented with vitamins. B₁-lactol* and powdered charcoal were administered orally and protein hydrolysate and dextrose were administered intravenously. Twenty-five milligrams of testosterone propionate was administered intramuscularly once a day for fifteen days. The patient's weight increased to 118½ pounds (51 kg.). He gained strength and his physical condition improved generally. He continued to have from 18 to 20 bowel movements each day. After the treatment had been continued for some time, the percentage of fat in his stools became normal. The patient was dismissed on May 30, 1947. He was advised to take plithalylsulfathiazole and to continue the treatment that had been prescribed at the Clinic. The patient's condition has not been satisfactory since he returned to his home. When this paper was written, the advisability of performing an ileostomy was being considered.

In view of the large portion of the intestine that had been removed in case 4 and since active ulcerative colitis, severe emaciation and steatorrhea were present, it is remarkable that hematologic examination did not disclose the presence of anemia. It is possible that the severe diarrhea caused chronic impairment of the fluid balance and that the resulting hemoconcentration masked the presence of anemia. The low concentration of ascorbic acid in the plasma is significant.

CASE 5—A salesman, aged 41 years, came to the Clinic on December 31, 1946 because of intermittent abdominal cramps, bloating and diarrhea. In January, 1943, while en route to the South Pacific with the Sea Bear, he had

*This is a proprietary preparation which is supplied in the form of tablets. Each tablet contains 1½ gram (0.00005 gm.) of bellafoline (true levorotatory alkaloids of fresh belladonna leaves, in the form of amine acid salts) and ½ gram (0.05 gm.) of phenobarbital.

had a sudden attack of diarrhea. He had passed from 10 to 12 stools per day and the stools had been watery, foul, foamy and light colored. The bowel movements had been accompanied by mild bloating and abdominal cramp.

In February 1943, he had been hospitalized for malaria and dengue. He had been told that his diarrhea was due to amebic dysentery but he had not been told whether or not *Endamoeba histolytica* had been found in his stools. Administration of bismuth salts had controlled the diarrhea. After he had been comparatively well for a few weeks, the diarrhea had recurred and had become uncontrollable. The diarrhea had been accompanied by general abdominal bloating and tenderness, and he had lost 30 pounds (13.7 kg.) by August, 1943. He had been hospitalized again, and a diagnosis of sprue had been made in September 1943. He had been evacuated to a naval hospital in this country. He had received a high protein diet which was supplemented with vitamins, bananas and other fruits. Iron also had been administered. He had returned to active duty in February 1944 but the former symptoms had recurred after he had eaten navy rations for a short time. He had been hospitalized on several occasions thereafter but he had not obtained permanent relief. In February 1945, he had received a medical discharge because of sprue.

Since his discharge he had had recurrent attacks of constipation. The constipation had been accompanied by abdominal tenderness and distention and by cramp which was situated in the middle of the abdomen. These symptoms had been followed by a period of diarrhea during which 10 to 12 large foamy, watery stools had been passed in about four hours. For a short time before the patient came to the Clinic, cramps had occurred in the course of the attacks.

Although the patient's normal weight was 190 pounds (86.3 kg.), he weighed only 164 pounds (74.4 kg.) when he came to the Clinic. His abdomen was moderately distended and peristalsis was audible. No masses could be felt in the abdomen. Palpation of the abdomen produced a splashing sound and percussion elicited a tympanic note. In the course of roentgenologic examination of the abdomen, retrograde filling of the terminal portion of the colon revealed that this segment of the intestine led directly to the left upper quadrant of the abdomen, where there was a large collection of gas. The roentgenologist expressed the opinion that the patient probably had an obstructive lesion of the small intestine.

The patient was hospitalized and medical treatment was instituted. A Miller-Abbott tube was inserted through the patient's nose and attached to a suction apparatus in order to decompress the distended intestine.

The value for the hemoglobin was 15.3 gms. per 100 cc. of blood. The erythrocyte count was 4,770,000 and the leukocyte count was 8,000. Examination of blood smear did not disclose any abnormality. The sedimentation rate of the erythrocytes was 11 mm. in one hour and the prothrombin time was 12.5 minutes. Analysis of the blood showed blood sugar, 107 mgm. phosphorus,

3.5 mg per 100 cc. of serum protein, 7.5 gm per 100 cc of serum, and serum amylase 80 Somogyi units per 100 cc. The albumin-globulin ratio of the serum was 1.8:1. A glucose tolerance test did not disclose any significant abnormality. Analysis of the gastric contents by the method of Tüpfel revealed that the acids for the free hydrochloric acid and total acidity were 34 and 44 respectively. Fat composed 9.1 per cent of the dry weight of the feces.

Röntgenologic examination of the small intestine revealed marked dilatation of the jejunum and an obstructive lesion high in the ileum. Exploratory laparotomy disclosed rather marked dilatation of the small intestine. The dilatation began about 2 feet (61 cm.) below the ligament of Treitz and was most pronounced in the last 4 to 5 feet (122 to 152 cm.) of the ileum. Definite torsion was present in the ileocecal region.

A Widal type of enterostomy was performed in the lower part of the ileum. The postoperative course was erratic. Because of severe stony of the intestine, it was necessary to irrigate the intestine with a double lumen tube in order to maintain decompression. Various supportive measures were employed. By the middle of February the patient was comfortable, was eating well and was passing stools normally. At that time, the stools had a fatty appearance. Although episodes of intestinal obstruction occurred occasionally the patient

per cent of the dry weight of the feces consisted of fat. Administration of pancreatin produced some subjective relief.

Another episode of intestinal obstruction occurred on March 23. On March 27 the patient attempted to irrigate his intestine through the enterostomy tube, as he had done many times before. A short time later severe pain occurred in his abdomen and the patient went into a state of shock. Röntgenologic examination disclosed torsion.

after the onset of the attack.

Necropsy disclosed 2,500 cc. of foul fluid in the abdominal cavity. The small intestine was enormously distended; some of the loops were 9 cm. in diameter. The omentum tapered down to form a thick cord which, after it had looped once around the base of the mesentery of the small intestine, was

In case 5 the signs and symptoms of intestinal obstruction closely simulated those of sprue for more than two years. The obstruction then pursued a fulminating course which was characterized by typical

had a sudden attack of diarrhea. He had passed from 10 to 18 stools per day and the stools had been watery, foamy and light colored. The bowel movement had been accompanied by mild bloating and abdominal cramp.

In February 1943, he had been hospitalized for malaria and dengue. He had been told that his diarrhea was due to amebic dysentery but he had not been told whether or not *E. histolytica* had been found in his stool. Administration of bismuth salts had controlled the diarrhea. After he had been comparatively well for a few weeks, the diarrhea had recurred and had become uncontrollable. The diarrhea had been accompanied by general abdominal bloating and tenderness, and he had lost 50 pounds (22.7 kg.) by August, 1943. He had been hospitalized again, and a diagnosis of sprue had been made in September 1943. He had been evacuated to a naval hospital in this country. He had received a high protein diet which was supplemented with vitamins, bananas and other fruits. Iron also had been administered. He had returned to active duty in February 1944, but the former symptoms had recurred after he had eaten navy rations for a short time. He had been hospitalized on several occasions thereafter but he had not obtained permanent relief. In February 1945, he had received a medical discharge because of sprue.

Since his discharge he had had recurrent attacks of constipation. The constipation had been accompanied by abdominal tenderness and distention and by cramp which was situated in the middle of the abdomen. These symptoms had been followed by a period of diarrhea during which 10 to 15 large foamy, watery stools had been passed in about four hours. For a short time before the patient came to the Clinic, emesis had occurred in the course of the attacks.

Although the patient's normal weight was 100 pounds (45.4 kg.), he weighed only 164 pounds (74.4 kg.) when he came to the Clinic. His abdomen was moderately distended and peristalsis was audible. No masses could be felt in the abdomen. Palpation of the abdomen produced a splashing sound and percussion elicited a tympanic note. In the course of roentgenologic examination of the abdomen, retrograde filling of the terminal portion of the ileum revealed that this segment of the intestine led directly to the left upper quadrant of the abdomen, where there was a large collection of gas. The roentgenologist expressed the opinion that the patient probably had an obstructive lesion of the small intestine.

The patient was hospitalized and medical treatment was instituted. A Miller-Abbott tube was inserted through the patient's nose and attached to a suction apparatus in order to decompress the distended intestine.

The value for the hemoglobin was 15.2 gm. per 100 cc. of blood. The erythrocyte count was 4,700,000 and the leukocyte count was 8,000. Examination of a blood smear did not disclose any abnormality. The sedimentation rate of the erythrocytes was 11 mm. in one hour and the prothrombin time

— qualitative analysis of the blood
— 100 cc. of blood sugar 107
— 100 cc. of serum phosphorus,

low weight. Progressive anemia had developed and blood transfusions had been administered.

When the patient was examined at the Clinic, he weighed 77 pounds (34.9 kg). With the exception of clubbing of the fingers, the physical findings were essentially normal. The value for the hemoglobin was 10.1 gm per 100 cc of blood. The erythrocyte count was 3,300,000 and the leukocyte count was



Fig. 223—*a*, Narrowing of jejunum immediately above the structure in case 5; *b*, Section of normal jejunum below the structure.

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removal of a large segment of the jejunum and all of the ileum, the jejuno-colic anastomosis was disconnected and the continuity of the jejunum was re-established. A subileal enteritis was noted in the distal portion of the ileum. The ileum was divided at the

end of the lower segment
removed to the transverse c

1939 His condition was satisfactory for about one year after the operation

signs and symptoms. The intensity of the stridor was evidently varied from time to time.

CASE 6—A boy aged 11 years, was brought to the Clinic on December 8, 1938. Two years previously he had begun to have abdominal cramp which had been characterized by remissions and exacerbations. Diarrhea had de-



Fig. 218—Enlargement and widening of the ileum—short distance above the ileocecal junction in case 6.

veloped one year later. The number of stools had increased gradually until he was having from 5 to 10 bowel movements each day. Vomiting had occurred

abdominal cavity. The postoperative course had been unremarkable. The cramp and diarrhea had not been relieved and the patient had continued to

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and
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The animals are able to absorb all foodstuffs and there is a considerable increase in the absorption of carbohydrates. The animals appear normal but they are very sensitive to unfavorable dietary and environmental conditions.

The compensatory process is characterized by hypertrophy and hyperplasia of the remaining portion of the intestine proximal to the site of the resection. Neither the stomach nor the portion of the intestine distal to the site of the resection undergoes any change. The diameter of the portion of the intestine involved in the compensatory process increases and it may become twice as large as normal. There also is an increase of as much as 400 per cent in the absorptive surface of the involved portion of the intestine. It appears likely that this increase in the absorptive surface approaches the epithelial area of the curved portion of the intestine. This compensatory process also has been observed in human beings who have undergone massive resection of the intestine.^{12, 13}

The amount of human intestine that can be resected without causing serious sequelae or death varies greatly in different cases.^{14, 15} The literature contains reports of cases in which patients have lived after the removal of more than 500 cc. of the intestine.^{16, 17} In some cases, excision of a relatively small portion of the intestine has been followed by severe metabolic disturbances.¹⁸

Resection of the small intestine of human beings is followed by many sequelae. Diarrhea is the most frequent sequela.^{19, 20, 21, 22} It is associated with an excessive loss of fat, protein and electrolytes in the feces.^{23, 24, 25, 26} This abnormality may be so severe and intractable as to interfere greatly with bodily nutrition and it even may cause death.²⁷ The diarrhea is aggravated by the inclusion of an excessive amount of fat in the diet. Anemia of various types,²⁸ loss of weight, edema,²⁹ tetany,³⁰ and pernicious vomiting are other sequelae that may occur. There also may be a decrease in the concentration of calcium³¹ and protein³² in the serum.

found that recognizable metabolic disturbances occurred in 27 of 38 cases.

Jordan and Bockus have said that resection of the small intestine for regional enteritis will not cause any physiologic derangement if the patient follows a proper dietary regimen after the operation. It has

In December 1930, abdominal fullness, tenderness and cramp developed after the patient had had an infection of the upper part of the respiratory tract.

The patient returned to the Clinic in February 1940. Roentgenologic examination disclosed what appeared to be a rather marked deformity of the cecum and ascending colon. The roentgenologist expressed the opinion that the deformity possibly was due to a hyperplastic process. Operation disclosed several patches of enteritis in the midportion of the jejunum. A portion of the jejunum 50 cm. long was excised and side-to-side anastomosis was performed. Examination of the surgical specimens revealed patches of subacute ulcerative enteritis which were separated by comparatively normal tissue. Microscopically the lesions resembled the lesions of sarcoidosis. The patient was dismissed on March 7 1940.

The diarrhea persisted after the patient returned to his home. The number of stools increased steadily until the patient was having as many as 24 bowel movements per day. The diarrhea was not associated with pain, chills or fever. When the patient returned to the Clinic on June 1 1945, he weighed 100 pounds (45.4 kg.). The results of physical examination were not particularly significant. Clubbing of the fingers was not observed at this time. The value for the hemoglobin was 16 gms. per 100 cc. of blood. The erythrocyte count was 4,550,000 and the leukocyte count was 9,900. Quantitative analysis of the blood disclosed the following values: urea, 28 mg. per 100 cc. of

serum (15 cm.) of the terminal portion of the ileum. There was no evidence of stricture at the site of the ileocolic anastomosis.

The patient was placed on a high caloric diet which contained a normal amount of fat. Two cubic centimeters of campolon (crude liver extract)* was administered intramuscularly every other day. One week after the treatment the number of stools had decreased to 1 per day. In three

COMMENT

Experiments on animals have demonstrated that the immediate effect of the administration of a high caloric diet to animals is a rapid gain in weight. When animals are fed a rich, easily assimilable diet, digestion becomes normal.

Each cubic centimeter of this preparation represents 0.05 G.P. metabolizable units of liver extract.

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been stressed repeatedly that the diet should contain a relatively large amount of protein and carbohydrate and a small amount of fat.^{11, 12} It is interesting to note that the results of resection of the intestine were unsatisfactory in 4 of the 12 cases of regional ileitis reviewed by Jordan. Some degree of abdominal distention occurred in 3 of the 4 cases and an unspecified type of diarrhea occurred in the remaining case.

After resection of the small intestine the physical condition of the patient appears to depend on the following factors: (1) the pathologic conditions which necessitated the resection; (2) the length and physical condition of the remaining portion of the intestine and the extent to which it is able to compensate for the resection; (3) the resistance of the patient; and (4) the type of dietary regimen that is instituted after the operation.^{11, 12, 13}

The wide variation in the manner in which different patients react to resection of the intestine is illustrated by case 1, in which resection of only 2 feet (61 cm.) of the midportion of the jejunum resulted in moderately severe steatorrhea and by case 3, in which the resection of 105 cm. of the midportion of the jejunum caused only a slight change in the patient's tolerance for dextrose and a minimal degree of steatorrhea. Cases 2 and 4 are illustrative of the severe disturbances that may be caused by resection of the intestine.

The deficiency state did not follow a fixed pattern in the cases which we have reported. In cases 1 and 3 the insufficiency involved only one or two dietary principles but in cases 2, 4 and 6 it produced a diffuse metabolic disturbance. In cases 2, 3 and 6 microscopic examination revealed that the lesions resembled the lesions of sarcoidosis. This would seem to indicate that severe jejuno-ileac insufficiency is likely to develop in cases in which the lesions are of this type.

SUMMARY

This paper is based on a study of a large number of patients with jejuno-ileac insufficiency with a report of 6 illustrative cases. The amount of small intestine that can be removed or isolated without producing signs and symptoms of a deficiency disease varies greatly in different cases. The development of the deficiency state also is influenced by the type of dietary regimen that is employed after the operation. The symptoms depend on the nutritional factors that are involved.

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THE CARE AND PREVENTION OF DECUBITUS ULCERS

ELWYN S. SHONTO

In the initial phases of treatment the paraplegic patient needed co-ordinated attention from more medical specialists than any other war casualty. Evaluations were necessary from the orthopedic surgeon regarding the fracture of the vertebra, from the neurosurgeon regarding the injury to the spinal cord, from the internist regarding the severely depleted nutritional state of the patient and the dietary control of involuntary defecation, from the urologist regarding the atonic urinary bladder and the ever-present danger of ascending infection of the urinary tract, from the psychiatrist and occupational therapist regarding the important problem of mental adjustment to a new and limited form of living, and from the surgeon regarding the care and prevention of decubitus ulcers.

It is the purpose of this article to deal only with the problem of decubitus ulcers and to present a general description of care and prevention based on my experience in the armed forces with these ulcers in paraplegic patients. Much was learned during the course of the war regarding the care of decubitus ulcers and it is of interest that similar principles of treatment were evolved independently in various army hospitals.^{1, 2-5}

The problem of decubitus ulcers roughly has three phases: (1) prevention, (2) conservative treatment, and (3) surgical treatment.

PROPHYLAXIS

Prophylaxis for either occurrence or recurrence of decubitus ulcers can be reduced to the two principles of avoidance of prolonged pressure (not more than two to three hours) over any part of the body¹ and of either increasing or maintaining the nutritional state of the patient.

Without proper nutrition for without it, all attempts at either prophylaxis or treatment fail. The morale of the patient is of prime importance in maintaining proper nutrition, for loss of appetite from discouragement and anxiety cannot be countered for long merely by tonics and parenteral feedings. I found determinations of concentrations of hemoglobin and serum

From experiences gained while Major Shonto

serving in the armed forces.

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THE CARE AND PREVENTION OF DECUBITUS ULCERS*

ELWYN S. SHOCKO

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It is the purpose of this article to deal only with the problem of decubitus ulcers and to present a general description of care and prevention based on my experience in the armed forces with these ulcers in paraplegic patients. Much was learned during the course of the war regarding the care of decubitus ulcers and it is of interest that similar principles of treatment were evolved independently in various army hospitals.¹⁻⁴

The problem of decubitus ulcers roughly has three phases: (1) prevention, (2) conservative treatment, and (3) surgical treatment.

PROPHYLAXIS

Prophylaxis for either occurrence or recurrence of decubitus ulcers can be reduced to the two principles of avoidance of prolonged pressure (not more than two to three hours) over any part of the body¹ and of either increasing or maintaining the nutritional state of the patient in order that the subsequent increase in the subcutaneous fat pad and a more healthy skin will buffer such pressure and trauma as are unavoidable. One cannot stress too much the problem of proper nutrition, for without it, all attempts at either prophylaxis or treatment fail. The morale of the patient is of prime importance in maintaining proper nutrition. For loss of appetite from discouragement and anxiety cannot be countered for long merely by tonics and parenteral feedings. I found determinations of concentrations of hemoglobin and serum

*From experiences gained while Major Shockey was serving in the armed forces.

protein valuable adjuncts in determining the over-all nutritional state of the patient in the early phases of treatment¹⁻⁴ but the body weight curve proved to be more dependable in the long run in any cases.

Other factors in prevention of ulcers include frequent turning of the patient, provision for soft surfaces under the pressure points of the body in order to dissipate the body weight over a larger area and proper hygiene to prevent contamination and maceration of the skin from moisture and excrement.

CONSERVATIVE TREATMENT

On admission to the hospital within the zone of the interior paralyzed patients usually weighed less than 100 pounds (45 kg.) and had bed sores over the various bony prominences of the body. The majority of these occurred over the sacrum and trochanters but smaller ulcers often were found over the spinous processes, scapulae, elbows, heels and knees.

In addition to the program of prevention of further ulcerations just outlined, conservative treatment consisted primarily of mechanical and chemical debridement followed by dressings which created the least possible irritation to the denuded surface. Chemical debridement with Carré Dakin solution applied as wet packs every three hours with zinc oxide or aluminum ointment to protect the surrounding skin resulted in a clean granulating wound within a few days, provided that the patient's nutritional status was satisfactory. The lesion then began to shrink both from ingrowth of new epithelium and from contracture of underlying scar tissue. Controlled observations were made as to the effects of various pastes, ointments, oils and solutions on the rate of healing but no definite direct stimulating effect could be observed from any local treatment. The greatest stimulation of healing in these cases consisted of removal of all irritating and toxic elements from the wound surface in order that normal reparative processes could proceed unhindered.

After debridement the wounds were left open to the air and sunlight

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cessive trauma subsequently healed satisfactorily by this treatment alone but as in the experience of others,³⁻⁵ ulcers over the sacrum and trochanters were usually too large and subject to too much trauma to be healed permanently by conservative methods.

SURGICAL TREATMENT

The surgical phase of treatment which proved most useful consisted of two fundamental procedures: 1. Free split thickness grafts of the "postage stamp" type fixed in place by the thromboplastin technique, were satisfactory for the closure of large superficial ulcers when the loss of body fluids from the raw surface was excessive.^{1, 4} This procedure was adequate as a final stage in most cases except in cases of sacral ulcers in which the lack of a subcutaneous fat pad resulted in an ultimate break down of the graft as soon as the patient was able

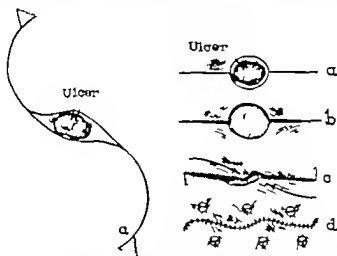


Fig. 944.—Two types of closure. *a'* One of the simpler classical methods of closure. *a, b, and c* The steps of the modified procedure used by the author. There is no loss of normal skin in *a'* and the tension and surgical undermining are much less for ulcers of equal size.

to get around in a wheel chair and in cases of trochanteric ulcers in which the extensive undermining along the *fascia lata* did not permit this type of procedure. This procedure was not abandoned in the treatment of large sacral decubitus ulcers, however, because these grafts could be preserved with restricted ambulation until a more permanent type of closure could be performed. The advantage of using split thickness grafts as an intermediate stage for sacral ulcers was (1) to remove the large oozing and devitalizing lesion as early as possible and (2) to allow the denuded region to shrink in size. This shrinkage which often resulted in a decrease of as much as 30 per cent of the size of the

region made subsequent excision and closure by the sliding technique much easier. The other procedure used in surgical treatment in my cases was a sliding surgical closure. The simplest surgical method



Fig. 144—*a*, Ulcer over tracheostomy before operation. *b*, Same two weeks after operation. The excised skin measured 11 by 14 cm. and was closed by the method in Figure 144. The modified procedure was developed later and could have lessened the extensive procedure considerably. Approximately half of the incision is seen in this photograph, the other end of the incision is in the left axillary region.

which will achieve optimal results is always the method of choice. The sliding closure in my cases gave the best results because it preserved and made use of all possible normal skin in the region of the ulcer, gave a nearly straight line closure and permitted a change to a more radical procedure during the course of the operation if necessary. The

straight line closure minimizes surgical scar brings in a subcutaneous fat pad to protect the skin against trauma which decreases the opportunity for subsequent recurrence of the ulcer and leaves the operative field clear for additional surgical procedures if the ulcer recurs at a future date.

The sliding technic is illustrated in Figure 244. One of the classical rotation flap methods of closure of epithelial defects is shown in Figure 244a' but, because of the loss of a triangle of skin from each side of the defect, a much longer incision than in the sliding closure is necessary and the undermined tissue is more extensive. This limits materially the size of defect which can be closed by this method. The modification of this procedure illustrated in Figure 244a to d is the sliding



Fig. 244—*a*, Ulcer over trochanter before operation. *b*, Scar four days after operation. The excised ulcer and scar measured 10 by 12 cm. and healed per primam. The postoperative scar is nearly straight.

technic which was employed. There is no loss of skin adjacent to the defect and the two angles, as illustrated by arrows, are used to fill in

through large buttons are placed at an angle to splint the skin margin in proper position and to remove all tension from the suture line.

The skin is held in approximation with interrupted silk sutures which are removed in three to four days. Penrose drains are placed either at the ends of the incision or through stab wounds and are left in place for about six days after operation. Penicillin also is administered by intramuscular injection for about seven days after operation.



Fig. 117—*a*, Ulcer over trochanter before operation. *b*, Same three weeks after operation. The excised ulcer and scar measured 9 by 9 cm.



Fig. 118—*a*, Sacral ulcer. *b*, Same four days after closure. The defect after excision of ulcer and scar measured 16 cm. in diameter. Healing was complete by the 15th day.

In cases in which decubitus ulcers over the trochanter were closed by this method, the patient was placed on a bityker frame for fourteen

days after operation in order to keep the thigh from flexing while the patient was being turned. This helped to splint the incision over the hip until the wound had healed adequately.



Fig. 118—*a*, Heel ulcer before operation. *b*, Heel twelve days after closure. The defect after excision of ulcer and scar measured 14 cm. in diameter and healed per primam.



Fig. 120—Unfavorable result. Infection sometimes follows radical advancement of flap to close decubitus ulcer. T flaps are rotated to cover the defect and the donor sites apparently received split thickness skin graft. When the patient arrived at this hospital the donor sites had begun to erode and within 1 month the flaps had become shriveled and detached.

More radical procedures are rarely indicated but if they become necessary this method of closure can be converted into one of more radical rotation or advancement as reported by Gibbon and Freeman and Croce and associates.⁸ When a more radical approach is necessary

the procedures just described seem preferable to any in which the skin flap is swung from a nearby donor site because a flap large enough to cover a defect, which cannot be closed by the simple sliding technique, will have a donor site so large that it cannot be closed primarily. A split thickness graft to this donor site is likely to break down at a future date. I have seen two cases in which the transposed flaps themselves have become detached several months after apparently successful closure of trochanteric decubitus ulcers (Fig. 250). This might be explained by the fact that the shape of the incision and excessive undermining increased the severity of an already embarrassed circulation in the paralyzed tissues. This plus the gradual contracture of excessive postoperative scar which was activated by the more radical procedure and by constant traction of the flap as the thigh was flexed further decreased the circulation in the flap until slough occurred.

SUMMARY

Care of decubitus ulcers can be considered in three phases: (1) prevention, (2) conservative management and (3) surgical closure. Prevention aims at proper nutrition and avoidance of trauma. Conservative management is usually adequate except for large ulcers or those over the sacrum and trochanters. The optimum in spontaneous closure can be obtained by maintaining proper body nutrition and avoidance of irritation to the denuded area. Surgical closure by split-thickness skin grafts are adequate for most large shallow ulcers which have been prepared properly. Exceptions are ulcers over the sacrum, which are exposed to undue trauma during ambulation, and ulcers over the trochanters which are usually deeply undermined. Split-thickness skin grafts can be useful in closure of large sacral decubitus ulcers, however as a preliminary step to subsequent excision and closure.

A method of simple excision and sliding surgical closure for ulcers over the sacrum and trochanters has been devised. This is adequate in all but extreme cases and allows optimal results with only a minimum of postoperative scar. This type of closure produces healing which can withstand the necessary trauma incident to ambulation better than the healing which follows more complicated procedures, and if some accident should cause a recurrence of the ulcer the surgeon is not hampered by excessive surgical scar in effecting a second closure.

The author is indebted to Drs. Frank C. Mann, Gordon B. New and associates for training which made a successful solution to this problem possible.

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CLINICS ON OTHER SUBJECTS

THE ASSOCIATION OF CARCINOMA OF THE THYROID GLAND AND EXOPHTHALMIC GOITER*

JOHN DEJ PEMBERTON AND B MARDEN BLACK

THE supposed rarity of the association of carcinoma of the thyroid gland and exophthalmic goiter has been widely accepted almost from the time that microscopic examination of thyroid glands became common practice.¹¹ The observation was largely of academic interest as long as the treatment of exophthalmic goiter remained surgical. However during recent years, since many patients suffering from exophthalmic goiter are being treated by nonsurgical methods, and since the question of carcinogenesis has been raised in connection with the drugs being used (propylthiouracil, radioiodine) the frequency of the association of the two conditions becomes of some practical importance. The question has already been raised in the literature whether thiouracil therapy was responsible for the development of a papillary adenocarcinoma in the thyroid gland of a patient with exophthalmic goiter whose preoperative preparation included thiouracil.¹²

Comments in the literature concerning the frequency of the association of the two conditions are not entirely consistent. While large numbers of thyroid glands removed because of exophthalmic goiter have been examined without carcinomas being found the microscopic examination of even moderately large numbers of thyroid glands

thyrotomies was insurance against cancer of the thyroid¹³ or "the incidence of carcinoma in diffuse exophthalmic goiter is practically zero" or "cancer is almost unknown in exophthalmic goiter"¹⁴ are not borne out by studies of series of cases of carcinoma of the thyroid gland. One of the 276 carcinomas of the thyroid gland reported by Pemberton in 1938, 1 of the 90 reported by Collier,¹⁵ 4 of the 226 reported by Clute and Warren¹⁶ and 1 of the 168 in Ward's series¹⁷ were found in the thyroid glands of patients who had exophthalmic goiter.

*Read at the meeting of the American Association for the Study of Goiter, Toronto, Ontario, Canada, May 6, 1949.

In a later report of Pemberton 10 of 774 carcinomas of the thyroid gland were found to have developed in thyroid glands removed because of exophthalmic goiter and Goetsch reported that 7 of a series of 52 carcinomas of the thyroid had developed "in the hyperplastic exophthalmic gland." Combining these figures, in 1.75 per cent of a collected series of 1,310 carcinomas of the thyroid gland, the malignant lesion had developed in the thyroid gland of a patient who had exophthalmic goiter.

Reports which would be more pertinent to the present study of the incidence of carcinoma in thyroid glands removed because of exophthalmic goiter are virtually nonexistent. Herbst did not find any carcinomas of the thyroid gland in 5,867 cases of exophthalmic goiter. Simpson similarly did not find any malignant lesions in 189 cases of exophthalmic goiter. Ward reported that the two conditions were associated in one instance in a series of 1,900 cases of exophthalmic goiter and Cole, Slaughter and Rosdter found the association once in 433 cases. Moore, Sweeney, Cope, Rawson and Means found a carcinoma in 1 of 53 patients with hyperthyroidism who had received thiouracil in preparation for surgical treatment. In a study of papillary adenocarcinomas of the thyroid gland seen at the Clinic from 1933 through 1945 one of us (Black) found that papillary adenocarcinoma was present in 0.4 per cent of the cases in which thyroidectomy had been carried out because of exophthalmic goiter during those years. It is evident that carcinoma of the thyroid gland does occur in association with exophthalmic goiter.⁴ It is equally evident that large numbers of thyroid glands which have been removed because of exophthalmic goiter may be examined and no carcinoma be found. This study was undertaken with the primary purpose of determining the incidence of the association of the two conditions in our material.

Apart from chance there is no ready explanation for the apparent rarity of the association of the two conditions. The assumption has been made that the hypertrophic or hyperplastic cell characteristic of exophthalmic goiter virtually never undergoes malignant transformation and that, consequently, the carcinomas found in thyroid glands involved by diffuse parenchymatous hypertrophy must have arisen in coincident adenomas. One of us (Pemberton) with Haines reported that the thyroid glands of 20 to 30 per cent of patients with exoph-

— Clute re-
with exoph-
— apted that

the majority of carcinomas of the thyroid glands develop as pre-existing

adenomas, or at least in nodular goiters² and it would be reasonable to suppose that similar changes would develop in adenomas situated in thyroid glands that are the seat of diffuse parenchymatous hypertrophy. One of us (Pemberton) found that in 4 of the 10 cases of carcinoma in thyroid glands removed because of exophthalmic goiter the carcinoma had developed in an adenoma. Clute reported that the carcinomas in all of his 4 cases had developed in adenomas and Goetach found evidence of a pre-existing adenoma in 3 of his 7 cases. Conversely in 6 of Pemberton's cases, in 4 of Goetach's cases and in the single case of Emmett and Dreyfuss and that of Payne, Crane and Price no evidence of a pre-existing adenoma could be found on careful microscopic examination. To account for the development of the carcinomas when no evidence of a pre-existing adenoma is found on microscopic examination, it has been assumed that the adenoma had been destroyed by the carcinoma. Goetach described certain cells which could be recognized in both the normal and the hyperplastic follicle which he considered to be fetal cells and which he suggested, could give origin to carcinoma primarily or through the stage of benign adenoma. While many of the carcinomas found in association with diffuse parenchymatous hypertrophy or hyperplasia have originated in coincident adenomas, there is little support for the conception that all such carcinomas originate in adenomas. Indeed, the objective evidence favors the view that not all originate in adenomas since meticulous study has failed to reveal adenomas in the majority of reported cases.

The question could also be raised, in view of the supposed rarity

merely a region of unusually exuberant papillary change which might possibly be observed in cases of exophthalmic goiter. The latter question will be discussed subsequently when the diagnosis of exophthalmic goiter in the present series is considered. The question of functioning and hyperfunctioning carcinoma of the thyroid gland is largely beyond the scope of the present paper. However it is known that carcinoma of the thyroid gland has no constant effect on the basal metabolic rate and that the majority of patients with the several varieties of carcinoma of the thyroid gland have normal or subnormal basal metabolic rates. Furthermore, when carcinomas of the thyroid gland and hyperthyroidism are found together there are usually histologic changes in the nonmalignant tissue to account for the hyper

In a later report of Pemberton 10 of 774 carcinomas of the thyroid gland were found to have developed in thyroid glands removed because of exophthalmic goiter and Goetsch reported that 7 of a series of 53 carcinomas of the thyroid had developed "in the hyperplastic exophthalmic gland." Combining these figures, in 1.75 per cent of a collected series of 1,510 carcinomas of the thyroid gland, the malignant lesion had developed in the thyroid gland of a patient who had exophthalmic goiter.

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Apart from chance there is no ready explanation for the apparent rarity of the association of the two conditions. The assumption has

involved by diffuse parenchymatous hypertrophy must have arisen in comorbid adenomas. One of us (Pemberton) with Haines reported that the thyroid glands of 20 to 30 per cent of patients with exophthalmic goiter seen in the Clinic contained adenomas and Clute reported that the thyroid glands of 8 per cent of patients with exophthalmic goiter contained fetal adenomas. It is generally accepted that the majority of carcinomas of the thyroid gland develop in pre-existing

ocal but the cases were included as cases of exophthalmic goiter because of the finding of diffuse parenchymatous hypertrophy in the extra-adenomatous tissue. The basal metabolic rate was elevated in every case ranging from +18 to +76 per cent, and the usual response was obtained after the administration of Lugol's solution (strong solution of iodine) to those patients who underwent operation since 1922. The hyperthyroidism of 3 patients was so severe that their operations had been carried out in stages. In 3 cases recurrent exophthalmic goiter had developed and the carcinoma was found in the tissues removed at the operations for the recurrence. In 2 of these 3 cases the original operation had been done at the Clinic and in neither case was there evidence of malignancy in the tissue which had been removed at the first operation. The usual histologic changes in the follicular cells seen with exophthalmic goiter were found in all but 4 cases and, in addition, other changes more or less suggestive of exophthalmic goiter were encountered frequently. These included particularly fibrosis, lymphocytosis and regenerative hyperplasia. Such findings would suggest that the thyroid glands in this series differed in no way from those usually removed because of exophthalmic goiter (Figs 251 and 252).

In 4 cases (cases 6, 7, 10 and 15) diffuse hypertrophy or hyperplasia of the follicular cells characteristic of exophthalmic goiter could not be demonstrated on careful macroscopic examination of the consistent benign thyroid tissue and the microscopic diagnosis in each of these cases was colloid goiter (Fig. 253). All 4 patients had been treated prior to operation with Lugol's solution (strong solution of iodine) and in each case the symptoms had been improved by this medication. The basal metabolic rates before operation were +25, +30, +53 and +62 per cent respectively and in each case the basal metabolic rate fell to normal after subtotal thyroidectomy. Coincident small adenomas were present in 1 of the 4 cases. In 3 of the 4 cases the symptoms were of such severity that the clinical diagnosis could not be seriously challenged while in the fourth case (case 15) the symptoms were mild and of short duration, the thyroid gland was not enlarged and the diagnosis of exophthalmic goiter could be questioned. This case has been included in the series solely on the basis of the clinical diagnosis. The resected thyroid tissue weighed 5 gm. only and the basal metabolic rate fell from a preoperative value of +25 per cent to +3 per cent twenty-two days after the operation. The symptoms of nervousness, tremor and slight intolerance to heat were relieved after the thyroidectomy and myxedema developed subsequently.

thyroidism. Recent studies of iodine uptake by carcinomas of the thyroid gland using radiiodine have revealed that usually the malignant tissue takes up far less iodine than does normal or particularly hyperfunctioning thyroid tissue.¹⁸ The collection of iodine is likely to be better the more differentiated the tumor but only occasionally do even papillary adenocarcinomas take up appreciable amounts of iodine. Such findings obviously lend support to the belief that the hyperthyroidism occasionally found in association with carcinoma of the thyroid gland more probably results from hyperfunction of the associated benign tissue than from hyperfunction of the malignant tissue.

PRESENT SERIES

The present series includes all patients seen at the Clinic from 1936

files have yielded 28 cases, which fell into two well-defined groups. In one group, numbering 15 cases, there was no evidence that the
 cases, in the

first group were observed during the last eleven years covered in the study. While the explanation for this is not entirely clear it probably is a reflection of an increased interest in the possible association of the two conditions, and consequent meticulous microscopic examination of all nodules observed in thyroid glands removed because of exophthalmic goiter. During the eleven year period, 1936 through 1946 approximately 3,500 operations for exophthalmic goiter were performed at the Clinic and in 15 cases carcinomas were found in the resected tissue, or a carcinoma was present in 0.4 per cent of the cases. The incidence is identical with that reported previously by one of us (Black) and serves as something of a check since the calculation was made from slightly different groups of cases.

The Diagnosis of Exophthalmic Goiter.—The diagnosis of exophthalmic goiter was made in all cases by members of the Section on Metabolic Diseases. In every case included in the series, with the possible exception of case 15, clinical hyperthyroidism was definitely present. In all but 2 cases the clinical diagnosis of exophthalmic goiter was unequivocal. In cases 18 and 28 the clinical diagnosis was equiv

carcinoma was recognized as such only on microscopic examination (Fig 254). In reviewing the tissues, we gained the distinct impression that in many cases such lesions can be recognized only if all nodules, however small, are sectioned and examined microscopically (Fig 255). Adenomas were present in the resected tissue in 12 of the 28 cases and in 7 of the 12 cases with adenomas the carcinomas had clearly originated in an adenoma. In the other 5 cases in which adenomas were found there was no evidence, on microscopic examination, that the



Thyroid
(H&E, 10x)

carcinoma had developed in an adenoma. In 10 of the 28 cases there were neither coincident adenomas nor evidence that the malignant lesion had developed in an adenoma. These findings are in accord with other reports previously mentioned. The carcinomas in the group in which there was no evidence that the malignant lesion had developed in an adenoma differed markedly from those in the group in which the carcinoma clearly had developed in an adenoma. This could be taken as further evidence that the malignant lesions in the two groups had had different origins and that the carcinomas in the first group had not developed in adenomas as those in the second group had done.



Fig. 351 (Case 3).—Diffuse parenchymatous hypertrophy. Columnar cells with papillary infolding are well shown (X113).

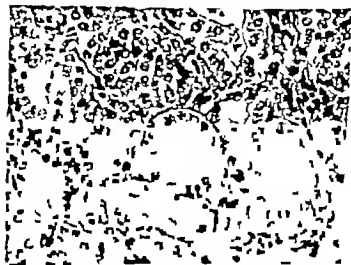


Fig. 352 (Case 4).—Diffuse parenchymatous hypertrophy (X300).

Malignant Throat.—As previously stated, the carcinoma was not suspected in any case before operation and in the majority of cases the

of the 14 cases the carcinoma had not spread beyond the thyroid gland. In 8 cases spread had occurred: in 1 the pretracheal muscles were involved by direct spread and, in the other, involvement of the homolateral posterior cervical lymph nodes was found at operation. In the remaining case in this group the lesion proved to be a diffuse adenocarcinoma, grade 4, which recurred locally within a few months of operation and which led to the patient's death two years after operation (Fig 255).

Since both papillary and diffuse adenocarcinomas develop from extra-adenomatous tissue, and since each of the two types of carcinoma is found with equal frequency among all cases of carcinoma of the thyroid gland at the Clinic, one could reason that while colloid



Fig 255 (Case 16)—Papillary adenocarcinoma, grade 1. The lesion could not be recognized grossly.

thyroid tissue gives origin to the two types of malignant lesions with approximately equal frequency, thyroid tissue involved by parenchymatous hypertrophy gives origin almost exclusively to the papillary variety. Such reasoning we believe is fallacious since it does not take into account the differences in clinical behavior of the two varieties of carcinoma. Diffuse adenocarcinomas of the thyroid gland are characteristically rapidly growing lesions. They usually cause definite symptoms and do not remain silent, so to speak, clinically. Papillary adenocarcinomas, conversely, tend to be small and they may remain undiagnosed for years, neither producing symptoms nor increasing appreciably in size. With these differences in clinical behavior in mind the question whether the hypertrophic or hyperplastic cell of exophthalmic goiter gives origin to carcinoma cannot be considered by studying the simultaneous association of the two conditions. Thus,

The cases comprising the first group exhibited considerable uniformity in that the lesions were papillary adenocarcinomas in 14 of



the 15 cases. The papillary lesions were considered as grade 1 (Broders method) in 12 cases and as grade 2 in 3 cases. In 5 cases the papillary lesions were multiple or at least multicentric. The papillary lesions in this group were all small with a mean diameter of 0.7 ± 1 mm. In 12

applied previously to the first group of cases could be similarly applied to this group. Malignant adenomas tend to be low grade and slowly growing and may be present for some time before symptoms are produced. Three of the 7 patients had had nodular goiters of moderate size and another patient had had a large nodular goiter for some time prior to the development of hyperthyroidism. No diffuse adenocarcinomas were found in the group and in none of the cases had the carcinoma spread beyond the thyroid gland or produced symptoms.

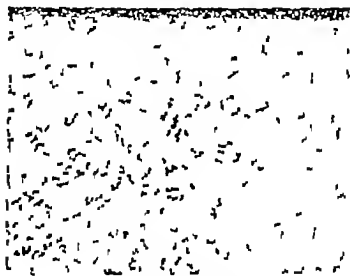


Fig. 257 (Case 18)—Adenocarcinoma, grade 2, in an adenoma. (X600)

REPORT OF CASES

Brief reports of the cases in the present series have been appended. In cases 6, 7, 10 and 15, as previously discussed, diffuse parenchymatous hypertrophy was not evident in the benign tissue. In cases 18 and 23, adenomatous goiter with hyperthyroidism could not be excluded with certainty on clinical grounds. These cases were included because of the diffuse parenchymatous hypertrophy in the extra-adenomatous tissue. The results of treatment were in keeping with those observed in other series of carcinomas of the thyroid gland. The cases were divided into two groups: (1) cases in which no histologic

in all cases in the present series tissue became available for microscopic study only because the patient had exophthalmic goiter. If the patient had not had exophthalmic goiter tissue would not have been available for study and, consequently the carcinoma would not have been discovered, at least as early as it was found. It is probable that the diffuse adenocarcinoma would have produced symptoms soon and it is equally probable that the enlarged lymph nodes in case 14 would have demanded biopsy but, in the remaining cases in the group, the carcinoma may have and probably had, existed for some time before



grade 2 (X100)

— It must be noted that the most severe lesions in thyroid tissue and which persists for years without symptoms, were present when exophthalmic goiter developed

In the second group of cases, in which the carcinoma had developed

— 2 of the 7 cases were malignant adenocarcinoma of the thyroid

exophthalmic goiter had developed eight years before he was seen at the Clinic. He stated that at that time he had been treated by means of rest and iodine and had made a partial recovery. He had never recovered completely, however, and all symptoms with the addition of those due to congestive heart failure had recurred about six months before he was seen at the Clinic. There was moderate exophthalmos with marked cardiac enlargement, atrial fibrillation and evidence of congestive heart failure. The basal metabolic rate was +41 per cent. The operation at the Clinic was carried out in stages. Left lobectomy was done first with removal of 60 gm. of thyroid tissue, which showed diffuse parenchymatous hypertrophy. Four months later the right lobe was resected, with the removal of 90 gm. of tissue which showed a diffuse adenocarcinoma, grade 4, resembling a sarcoma. Adenomas were also found in the resected tissue. In spite of the removal of the malignant tissue and irradiation, a hard, fixed recurrent lesion developed approximately four months after operation and the patient died as the result of the carcinoma two years after operation.

CASE 3—A woman 23 years of age had had typical symptoms of exophthalmic goiter for approximately one year. There were no ocular changes but the thyroid gland was moderately enlarged. The first basal metabolic rate determined at the Clinic was +76 per cent. After eleven days of preparation with Lugol's solution (strong solution of iodine) the basal metabolic rate had decreased to +37 per cent. Subtotal thyroidectomy was done with the re-

no evidence of recurrence on examination four years after the operation.

CASE 6—A woman 37 years of age had had the usual symptoms of exophthalmic goiter for one to two years. The symptoms had become more severe during the past two months and the patient had lost 16 pounds (7.3 kg.). There was no exophthalmos and the thyroid gland was not palpable clinically. The basal metabolic rate was +39 per cent. Subtotal thyroidectomy was carried out with removal of 10 gm. of tissue. The removed tissue showed only colloid thyroid in which there was a papillary adenocarcinoma, grade 1, 4 mm. in diameter. After operation the basal metabolic rate fell to normal and all symptoms disappeared. The patient was well six years after the operation.

CASE 7—A man 47 years of age had undergone thyroidectomy sixteen months before he was first seen at the Clinic. Prior to that operation he had had the usual symptoms of exophthalmic goiter and his basal metabolic rate was reported to have been +53 per cent. Lugol's solution (strong solution of iodine) had been prescribed preoperatively. The symptoms had not subsided after operation and had become somewhat more severe prior to his coming to

evidence could be found indicating that the carcinoma had developed in an adenoma (cases 1 through 18) (8) cases in which the carcinoma had clearly originated in an adenoma (cases 18 through 22) The assignment of numbers to the cases was entirely arbitrary

Group 1 Adenocarcinoma of Thyroid Gland and Exophthalmic Goiter Carcinoma Not in Adenoma

CASE 1—A man 35 years of age had had the usual symptoms of exophthalmic goiter for approximately two years The symptoms had become more marked during the last six months of this period The thyroid gland was enlarged moderately and the basal metabolic rate was found to be +45 per cent Subtotal thyroidectomy was carried out with the removal of 25 gm of tissue which showed diffuse parenchymatous hypertrophy There were two regions, each 4 mm. in diameter of papillary and solid adenocarcinoma, grade 1 in the resected tissue One small fetal adenoma was present in the gland, but no adenomatous tissue was present in the immediate vicinity of either region of malignant tissue

CASE 2—A woman 41 years old had had the usual symptoms of exophthalmic goiter for three years with considerable loss of weight and strength On physical examination atrial fibrillation was noted and the thyroid gland was enlarged The basal metabolic rate was +52 per cent Subtotal thyroidectomy was carried out with the removal of 30 gm of tissue which showed diffuse

CASE 3—The patient was a woman 69 years of age who had undergone thyroidectomy at the Clinic one year before for exophthalmic goiter Her basal metabolic rate prior to that operation had been +83 per cent Fourteen grams of tissue had been removed at operation The tissue showed diffuse parenchymatous hypertrophy with regenerative hyperplasia as well as several small adenomas The patient returned nine years later because all of the previous symptoms had recurred during the previous year The remnant of the thyroid gland had enlarged and the basal metabolic rate was +80 per cent

papillary adenocarcinoma, grade 1, the size of which could not be determined when the tissues were re-examined

CASE 4—The patient was a man 49 years of age Typical symptoms of

ried out with the removal of 20 gm. of tissue which showed diffuse parenchymatous hypertrophy with moderate thyroiditis. A papillary adenocarcinoma, grade 1, 7 mm. in diameter was found in the right lobe but no adenomas were present in the resected tissue. The patient is known to have been well one year after the operation.

CASE 12—A woman 52 years of age had had severe symptoms of exophthalmic goiter for approximately one year. The thyroid gland was enlarged and her basal metabolic rate was +65 per cent. Subtotal thyroidectomy was carried out with the removal of 19 gm. of tissue which showed diffuse parenchymatous hypertrophy with fibrosis and regions of regenerative hyperplasia, but no adenomas. There was one region of papillary adenocarcinoma, grade 1, 8 mm. in diameter in the left lobe. The patient was well two years after the operation.

CASE 13—A woman 45 years of age had had the usual symptoms of exophthalmic goiter for approximately 12 months. She had received iodine medication before she was seen at the Clinic. The thyroid gland was moderately enlarged and the basal metabolic rate was +43 per cent. Subtotal thyroidectomy was carried out, with the removal of 36 gm. of tissue which showed diffuse parenchymatous hypertrophy. A papillary adenocarcinoma, grade 1, 8 mm. in diameter and several adenomas were found in the resected tissue. There was no evidence that the carcinoma had arisen in adenoma.

CASE 14—A woman 25 years of age had had moderately severe symptoms of exophthalmic goiter for ten months. Unilateral exophthalmos was present and enlarged lymph nodes were found in the left posterior cervical triangle. The basal metabolic rate was +28 per cent. Subtotal thyroidectomy was carried out with the removal of 18 gm. of thyroid tissue. The enlarged posterior cervical lymph nodes were removed as a group. A papillary adenocarcinoma, grade 1, 10 mm. in diameter was found in the left lobe of the thyroid gland. Several lymph nodes were involved metastatically. The remaining thyroid tissue showed diffuse parenchymatous hypertrophy but no adenomas. The basal metabolic rate fell to -15 per cent after operation.

CASE 15—A man 55 years of age had noted nervousness, tachycardia and tremor for a few weeks only. The thyroid gland was not palpable but the basal metabolic rate was +25 per cent. Blood pressure was 102 mm. of mercury systolic and 60 diastolic and the pulse rate was 108 per minute. Subtotal thyroidectomy was carried out with removal of 5 gm. of tissue which showed colloid thyroid but no adenomas. There was a papillary adenocarcinoma, grade 1, 8 mm. in diameter in the resected tissue. The basal metabolic rate fell to +3 per cent after operation and myxedema subsequently developed. The diagnosis in this case is the least well supported in the group in that there was no histologic evidence of exophthalmic goiter and the symptoms were not particularly striking.

the Clinic. The thyroid gland was palpable and the basal metabolic rate as determined at the Clinic was +55 per cent. Subtotal thyroidectomy was carried out for what was thought to be recurrent exophthalmic goiter with the removal of 60 gm. of tissue which showed, however, only colloid thyroid tissue. There were three regions of papillary adenocarcinoma, grade 1 which measured 10 mm, 5 mm and 2 mm respectively; no adenomas were present. The basal metabolic rate fell to -3 per cent after the operation. The patient was well 3 years after the operation at the Clinic.

CASE 8.—A woman 37 years of age had had the usual symptoms of exophthalmic goiter for five months and had noted the presence of a goiter for one month. The eyes were slightly prominent and the thyroid gland was symmetrically enlarged. The basal metabolic rate was +51 per cent. Subtotal thyroidectomy was carried out with removal of 80 gm. of tissue which showed diffuse parenchymatous hypertrophy with some thyrotoxicity. A papillary adenocarcinoma, grade 1, 15 mm. in diameter was found in the resected tissue but no adenomas were found. The patient is known to have been well four years after the operation.

CASE 9.—A woman 48 years of age had had symptoms of exophthalmic goiter for approximately five months. She had had no symptoms of congestive cardiac failure although fibrillation was found to be present on examination at the Clinic. The thyroid gland was moderately enlarged and the basal metabolic rate was +67 per cent. Subtotal thyroidectomy was carried out with the removal of 30 gm. of tissue which showed diffuse parenchymatous hypertrophy. Two regions of papillary adenocarcinoma, grade 2, each 10 mm. in diameter were found in the resected tissue as well as several small adenomas. There was no evidence that either of the carcinomas had arisen in an adenoma. The patient was well three years after the operation.

CASE 10.—A woman 44 years of age had had typical symptoms of exoph-

Her basal metabolic rate when she was first seen at the Clinic was +64 per cent. Subtotal thyroidectomy was carried out with the removal of 50 gm. of tissue. Diffuse parenchymatous hypertrophy could not be found after extended study of the resected tissue. Several regions of papillary adenocarcinoma, grade 2, were found but there were no adenomas in the resected tissue. All symptoms were relieved completely after the operation. No information concerning the patient beyond the immediate postoperative period could be secured.

CASE 11.—A woman 30 years of age had had the usual symptoms of exophthalmic goiter for one year. The thyroid gland was slightly enlarged and the basal metabolic rate was +48 per cent. Subtotal thyroidectomy was car-

1.8 mm in diameter which had developed in an adenoma. The patient was well eleven years after the operation.

CASE 20.—A woman 30 years of age had had the usual symptoms of exophthalmic goiter for approximately eight months. The thyroid gland was moderately enlarged and the basal metabolic rate was +51 per cent. Subtotal thyroidectomy was carried out with the removal of 30 gm. of tissue which showed diffuse parenchymatous hypertrophy as well as multiple adenomas. One of the nodules proved to be a malignant adenoma, grade 2, 1.5 mm in diameter. The patient was well eleven years after the operation.

CASE 21.—A woman 19 years of age had had a goiter for approximately six years. Symptoms of hyperthyroidism had been present for five or six months. The goiter was clearly adenomatous and two determinations of basal metabolic rates gave values of +15 and +42 per cent. Subtotal thyroidectomy was carried out with the removal of 16 gm. of tissue. A papillary adenocarcinoma, grade 1, 2.5 cm. in diameter which clearly had originated in an adenoma and diffuse parenchymatous hypertrophy were found in the resected tissue. The patient was well approximately ten years after the operation.

CASE 22.—A woman 45 years of age had had obvious hyperthyroidism for one year. The thyroid gland was adenomatous and the basal metabolic rate was +34 per cent. Subtotal thyroidectomy was carried out with the removal of 80 gm. of tissue which showed diffuse parenchymatous hypertrophy. Multiple adenomas were present, one of which proved to be a malignant adenoma, grade 1, 2 cm. in diameter. This case was considered an exophthalmic goiter on the basis of the diffuse parenchymatous hypertrophy as the extra-adenomatous tissue.

SUMMARY

Carcinoma of the thyroid gland occurs occasionally in association with exophthalmic goiter. In a series of cases of carcinoma of the thyroid gland collected from the literature 1.73 per cent of the malignant lesions were associated with exophthalmic goiter. At the Clinic 0.4 per cent of the thyroid glands removed because of exophthalmic goiter from 1936 through 1946 contained coincident carcinomas. In all 22 such cases have been encountered at the Clinic. In 15 of the cases the malignant lesions had evidently not originated in an adenoma while in 7 cases, the carcinoma had developed in adenomas. The great preponderance of the fact that the symptoms appeared before the onset of the exophthalmic goiter in most cases. At least this explanation of the preponderance of low-grade lesions seems

Group 2. Adenocarcinoma of Thyroid Gland and Exophthalmic Goiter Carcinoma Developed in Adenoma

CASE 16—The patient was a woman 44 years of age. She had undergone operation at the Clinic eleven years previously for severe exophthalmic goiter with crisis. This operation had been done before Lugol's solution (strong solution of iodine) was used in the preparation of thyrotoxic patients for surgical treatment. Superior pole ligations had been carried out first, followed four months later by subtotal thyroidectomy. Eighty-seven grams of tissue had been resected, which showed diffuse parenchymatous hypertrophy. All symptoms had recurred and the left lobe had increased in size approximately two years previous to this visit. At this time the left lobe was definitely enlarged, there was marked exophthalmos and the basal metabolic rate was +30 per cent. This operation was limited to left lobectomy. A malignant adenoma, grade 3, 3 cm. in diameter was found in the resected tissue, which weighed 80 gm. The extra-adenomatous tissue showed diffuse parenchymatous hypertrophy. The patient was well nineteen years after the second thyroidectomy.

CASE 17—A woman 45 years of age had had severe symptoms of exophthalmic goiter for nine months. The basal metabolic rate as determined at the Clinic was +46 per cent. Subtotal thyroidectomy was carried out with the removal of 23 gm. of tissue which showed diffuse parenchymatous hypertrophy. There were numerous adenomas embedded in the substance of the gland, one of which proved to be a malignant adenoma, grade 1. The patient was well sixteen years after the operation. It was impossible to secure measurements of the carcinoma.

CASE 18—A woman 36 years of age had had typical symptoms of exophthalmic goiter for approximately one year. She was also suffering from pulmonary tuberculosis. She had received Lugol's solution (strong solution of iodine) prior to coming to the Clinic and the basal metabolic rate as determined at the Clinic was +19 per cent. Subtotal thyroidectomy was carried out with removal of 82 gm. of tissue which showed diffuse parenchymatous hypertrophy and multiple adenomas. One of the adenomas was considered to be a malignant adenoma, grade 2.

CASE 19—A woman 36 years of age had had a small goiter since adolescence. The goiter had increased moderately in size during the previous ten

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multiple adenomas. There was one region of papillary adenocarcinoma —

VOLVULUS OF THE CECUM

CLAUDE F. DIXON AND ALFRED C. MEYER

Among the rare but most urgent problems of intestinal obstruction are those occasioned by volvulus of the cecum. Because this condition is so infrequently considered and so infrequently diagnosed, the mortality rate attending it has been astonishingly high. The spectacular clinical and roentgenologic findings and the favorable results obtained with proper treatment have stimulated us to make a detailed analysis of this anomaly.

The first published report of volvulus of the cecum was that of Rokitanaky in 1841. Pagge in 1868 reported a case exhibited to the Pathological Society in 1850. He reviewed results of 4,000 consecutive necropsies at Guy's Hospital and found 54 cases of intestinal obstruction. Of these 4 were due to volvulus of the cecum. Firth in 1892 reported a case in which volvulus of the cecum was fatal, and Troves had collected 8 cases by 1900. Faltin assembled 79 cases in 1902. Ekshorn, Corner and Sargent, Bundschuh, Chalfant and Kuntz have added to this series, and Wolfer, Beaton and Anson finally brought the total number of cases to 194 in 1942. Interesting cases have also been reported by other investigators.^{1,2,3-11,12,13-21,22,23,24,25,26}

Early reports presented volvulus of the cecum as a pathologic curiosity found at necropsy. Until 1947 when Young and co-workers described 7 cases with but 1 death, the prognosis was grave. For instance, of the 57 patients reported on by Corner and Sargent in 1903, 38 died and 19 recovered, a mortality rate of 65 per cent. Also, Chalfant had assembled 119 cases by 1921. Of these, 96 patients were operated on and the fatality rate was 59 per cent, all 23 not operated on died making an over-all mortality rate of 67 per cent.

The etiology of volvulus of the cecum has been studied thoroughly. Homans stated, "As a *sine qua non* for the development of a twist of the right colon, it must have a long mesentery." Wolfer, Beaton and Anson in an accurate anatomic study of 125 adult cadavers, found that in 11.2 per cent the cecum was mobile enough to allow development of a volvulus. Any degree of incomplete rotation of the cecum, such as might result from a long mesentery which would allow the right portion of the colon to be displaced to the left side, furnishes the potential for a volvulus. The exciting cause may be anything which distorts the already mobile cecum. Instances of volvulus of the cecum have occurred in pregnancy^{1,2,27,28}, labor¹ and post partum.²² With-

more acceptable than the belief that the hyperplastic or hypertrophic cells give origin almost exclusively to papillary malignant lesions. The finding of a carcinoma in the thyroid gland of a patient who has received goitrogenic drugs or radiolodine does not imply an etiologic relationship between the drug and the malignant lesion.

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and feces. One of these a girl 7 years of age, had had almost daily attacks of pain since the age of 6 months. As stated before she had been operated on elsewhere at this early age for volvulus of the cecum. The other 2 patients had experienced symptoms for eighteen months and two years, respectively. These patients did not manifest pertinent abnormalities at the time of physical examination.



Fig. 430.—Highly distended cecum in the left portion of the abdomen; the cecum resembles the stomach in roentgenogram. Not gas-filled loops of small bowel, but absence of gas in remaining large bowel. (Clamp visible near top of figure is on T tube in the common bile duct.)

Roentgenograms of the abdomen were taken in 9 cases. In all instances of acute volvulus, distended gas-filled loops of bowel were observed, but in only 1 case was it suspected that one of the distended loops was cecum. Although ileus could be recognized in all cases, the exact site and type of obstruction were not apparent. In 5 of 9 cases a greatly distended loop of intestine was seen in the left side of the abdomen. It closely resembled the stomach in two instances, and twice it was thought to be sigmoid colon. The presence of gas-filled small intestine

drawal of packs from the abdomen after pelvic operation has been considered a cause. Miller and Clagett stated that other causes might be violent peristalsis following heavy purgation or overeating, abdominal tumors, mesenteric cysts, fecaliths, foreign bodies, direct violence and habitual constipation. Volvulus of the cecum may occur post-operatively.^{28,29} Sometimes it occurs for no discernible reason when the patient is asleep. Volvulus of the small intestine has been observed in the newborn.^{30,31}

Reports of 12 cases of volvulus of the cecum presented interesting diagnostic problems. Because of this and because the results of early surgical treatment were uniformly favorable we are presenting an analysis of these 12 cases. In each case the patient was operated on at the Clinic.

Volvulus was acute in 9 of the 12 cases and operation was an emergency measure. There were 3 cases of recurrent volvulus. One patient elected operation who had undergone emergency operation elsewhere for volvulus of the cecum at the age of 6 months, and in 1 case in which the patient was brought for emergency operation a previous elective operation had been performed for the same anomaly.

The oldest patient was 70 years and the youngest was 7 years of age; the distribution of patients over the intervening decades was fairly even. Eleven of the 12 patients had undergone at least one operation previously and strangely enough in 3 of them the operation was cholecystectomy. In 2 cases volvulus occurred in the immediate post-operative period.

The symptoms and signs were essentially those of intestinal obstruction. Severe intermittent colicky pains characterized the onset and were the chief complaint of all patients. The pain, although intense, was not located in any specific portion of the abdomen. In each patient, however, the pain remained localized in the sector of the abdomen in which it started. Pain occurred with about equal incidence in the various abdominal quadrants. Only 8 of the 12 patients experienced nausea and vomiting, and all but 4 were able to pass gas or fecal material after the onset of symptoms.

Physical examination revealed abdominal distention, tympanic to percussion, in all patients suffering from acute volvulus. In 4 instances there was a palpable mass which at operation, proved to be cecum.

Three patients were operated on in an interval between attacks. All had experienced similar attacks of pain previously but had been completely relieved, at least temporarily, by rectal elimination of gas.

cases the twist of the cecum involved other abdominal structures, in 1 the right fallopian tube, and in the other 5 fibrous bands of the abdomen. In 4 of these latter cases previous abdominal operations could have been responsible for the bands, but no previous abdominal operation had been performed in the other case. In 2 of the 12 patients operation for volvulus of the cecum had been performed seven years previously.



Fig. 100.—Distended cecum in pelvis. Preoperatively the cecum was thought to be sigmoid colon.

In all cases of acute volvulus, the cecum was hugely distended—so much so that in two instances the taenia coli had split, and in 2 other patients the wall of the cecum was gangrenous.

Detorsion was the primary step in treatment of volvulus in all cases. If

and the absence of a distended colon might, in retrospect, have suggested obstruction of the cecum but in no instance could a roentgenologic diagnosis be made definitely. However, not all of the roentgenologic diagnostic maneuvers, such as stereoscopic views and barium enemas, were used since the clinician believed surgical intervention was indicated on the basis of knowledge already acquired (Figs. 938 to 951).



Fig. 940.—Distended cecum lying in left part of abdomen. Gas-filled loops of small bowel may also be seen.

On exploration the cecum was found to have migrated to the right and the left portions of the abdomen with equal incidence. It occupied the pelvis and right lower part of the abdomen in 4 cases. It was associated with a tumor, in 1 case, and was cupped in 1 case.

While a long mesentery was present in each case, in only one instance was there enough congenital arrest in development to place the entire right portion of colon in the left part of the abdomen. In 6 of the 18

cases the twist of the cecum involved other abdominal structures in 1 the right fallopian tube and in the other 5 fibrous bands of the abdomen. In 4 of these latter cases, previous abdominal operations could have been responsible for the bands but no previous abdominal operation had been performed in the other case. In 2 of the 12 patients operation for volvulus of the cecum had been performed seven years previously.



Fig. 190.—Distended cecum in pelvis. Preoperatively the cecum was thought to be sigmoid colon.

In all cases of acute volvulus, the cecum was hugely distended—so much so that in two instances the taenia coli had split, and in 2 other patients the wall of the cecum was gangrenous.

Detorsion was the primary step in treatment of volvulus in all instances. If the loop was held by adhesions, it was necessary to sever

used and amputated over a three-bladed clamp. Because of extreme distention a Witte type of cecostomy was established in 1 case and an appendicostomy in another. The appendix was inflamed in two instances and consequently was removed.



Fig. 251.—Distended cecum in the left lower portion of abdomen. Gas-filled loops of small bowel lie above it. (Case of postoperative cholesty stasis; safety pins in the left upper abdomen are on Potters drains.)

In instances of chronic recurring volvulus of the cecum and ascending colon an operation was devised which proved entirely successful. After detorsion of the involved segment of bowel the peritoneal fold was freed on the lateral aspect of the mesentery and placed over the formerly twisted segment of bowel. The severed peritoneum was then sutured to the mesial portion of the mesentery. This operation placed the segment of bowel retroperitoneally and the fixation described prevented subsequent torsion (Figs. 252 and 253).

COMMENT

To compare the relative incidence of volvulus of various segments of the intestine Hilton reviewed all cases of proved volvulus at the Clinic between the years 1915 through 1948. Among the 88 cases, 64 (73 per cent) involved the small intestine, 7 (8 per cent) the cecum, and 17 (19 per cent) involved the sigmoid. In a recent report from

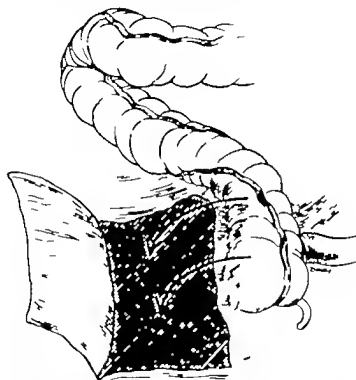


Fig. 282.—The retracted cecum is retracted medially on its long mesentery. The peritoneum, which covers the lateral aspect of the mesentery and the lateral peritoneal fold, is moved and elevated.

Scandinavian countries, Brunsgaard found that of 459 cases of volvulus of the large intestine, 141 (30 per cent) were of the cecum, 14 (3 per cent) were of the transverse colon, and 284 (63 per cent) involved the sigmoid. The relative incidence of volvulus of the cecum as compared to the sigmoid was about the same as that found at this Clinic.

Diagnosis depends first on the presence of intestinal obstruction and second on the recognition of a twisted cecum as the source of distress. The classic picture of abdominal distention accompanied by colicky pain is present in all cases of acute volvulus. Absence of nausea and vomiting in some instances and successful elimination of gas or feces from the rectum should not obscure the diagnosis of intestinal obstruction. Not only the fact that a large extent of small intestine lies above

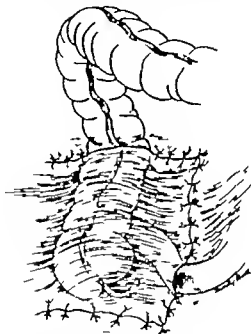


FIG. 983.—The cecum is returned to its normal position and the previously elevated peritoneum is sutured over the cecum to the medial aspect of its mesentery.

the site of volvulus but also the fact that there are several feet of colon below it accounts for these findings. In the presence of other findings, absence of nausea and vomiting and elimination of gas or feces by rectum are valuable aids in localizing the site of the lesion.

In the right quadrant of the abdomen, the abdominal examination does not reveal the cecum. In localization of the site and determination of the nature of the obstruction, roentgeno-

grams were of little value in the cases herein reported. Young and co-workers found the dilated cecum in the left upper quadrant in 90 per cent of their cases; this was associated with absence of a normal cecal outline in the right lower quadrant. In only 3 cases in our series however was a distended loop of bowel observed in the left upper quadrant of the abdomen and in only 1 case was it recognized as being cecum. Barium enema was used only in cases of chronic recurrence and in 2 of the 3 subjects abnormalities of the cecum were found. Young and co-workers used barium enemas even in the cases of acute volvulus and were able to demonstrate a dilated portion of bowel proximal to the point of obstruction of the barium column; no barium outlined the cecum in the right lower quadrant. They also observed at least the initial twisting and torsion of the mucosal pattern as outlined by barium, the wall of the bowel and gas. They too found that the dilated cecum may resemble the stomach. It is our impression that little is to be gained from the use of barium in such instances of acute obstruction and the danger of perforation is always present. If diagnosis of intestinal obstruction is clinical, roentgenograms of the abdomen may suggest the cecum by the enormity of the dilatation, the presence of gas in the small intestine and the absence of a gas-filled colon. Only rarely will all these symptoms be present.

Emergency operation is mandatory in cases of acute volvulus and procedures instituted should be as simple as possible. Simple detorsion and fixation if feasible offer the patient his best chance for recovery. If distention is excessive, cecostomy or appendicostomy is an effective emergency measure. Resection should be instituted only when the bowel or mesentery is no longer viable.

SUMMARY AND CONCLUSIONS

Twelve cases in which volvulus of the cecum was encountered at the Clinic were analyzed. In all cases failure of normal fixation of the cecum was manifested. Eleven of 12 patients had had previous operations, 10 of them abdominal; in 2 cases volvulus occurred in the immediate postoperative period.

The signs and symptoms of volvulus of the cecum are those of a low intestinal obstruction, but absence of vomiting and passage of gas and fecal material by rectum do not preclude diagnosis early in the disease.

Occasionally diagnosis of volvulus of the cecum may be made on roentgenographic examination. A hugely distended loop of large bowel is apparent and the presence of gas in the small intestine is evident but the colon is not distended.

Simple detorsion and fixation if possible are the best treatment in the absence of gangrene. Resection over a three-bladed clamp is the safest procedure when gangrene is present.

Intermittent volvulus of the cecum does occur. A new operative procedure is suggested for its correction.

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POSTGASTRECTOMY GASTRITIS

HOWARD A. GRAY, WARD C. MEYER, AND MALCOLM B. DOCKERTY

THE decision to submit a patient suffering from peptic ulcer to a partial gastrectomy is fraught with some anxiety inasmuch as the occasional patient who manifests a poor physiologic reaction to the procedure may have postoperative difficulties which are as serious or more serious than those which were present prior to the operation.

Browne and McHardy¹ said that the following complications may occur in cases in which partial gastrectomy has been performed: (1) recurrent or anastomotic ulceration, (2) hemorrhage from ulceration or gastritis, (3) edematous stomal obstruction resulting from ulceration, hypoproteinemia or gastrojejunitis, (4) hematopoietic disturbances, (5) motor and secretory dysfunction, reservoir loss, intubation abnormalities, digestive deficiency, gastrogenic diarrhea, (6) deficient absorption, particularly of iron and calcium, (7) manifestations of vitamin deficiency, (8) chronic jejunitis and (9) chronic gastritis. These authors have called attention to the fact that Schmuller considered chronic gastritis to be the most frequent gastric complication. This may be true; in fact, all the other listed complications, with the possible exception of motor disturbances and perhaps anastomotic ulceration, can be traced directly or indirectly to the factor of chronic gastritis.

Recurrent or anastomotic ulceration often is preceded by gastritis, either local or general. Hemorrhage occurs from an ulcer which has eroded a vessel, or it may result from generalized oozing from chronic hemorrhagic ulcerative gastritis. Ulceration or gastrojejunitis with associated edema in the region of the stoma may cause malfunctioning of the remnant of the stomach because of interference in mechanics and distressing symptoms due to alteration of physiologic processes. Such physiologic disturbances in digestion often will result in a number of more far-reaching and serious complications, such as hypoproteinemia, anemia, avitaminosis, and deficient absorption of iron and calcium. These generalized manifestations in turn have a further deleterious effect on the stomach and a vicious cycle of cause and effect is set up.

Schmuller has described a characteristic "purplish, red or claret colored, occasionally dark red" mucosa which is seen gastroscopically after resection of the stomach but Browne and McHardy expressed

the opinion that the color is related directly to the hematopoietic status of the patient. These observers have found that the post gastrectomy gastritis most frequently is a combination of the superficial and hypertrophic varieties. It involves the entire remnant but is more severe in the anastomotic area and extends into the jejunum as a *gastrojejunitis*. Achlorhydria is the rule. There is severe edema of the gastric rugae, the mucous membrane is turgescient and red, is often pitted with minute erosions and sometimes is covered with yellow-gray mucus. The furrows frequently are filled with purulent material.

Schindler has related the occurrence of gastritis to a stomal inadaptation or to bacteriologic factors, but he quoted Wanke who considered it to be a continuation of a presurgical status. Browne and McIlhenny have noted that the patient with achlorhydria has

a difficult rehabilitation period and who has an achlorhydria with its associated bacterial flora. In addition, the patient may have poor stomal function or inability to adjust to adequate dietary regulation.

Browne and McIlhenny have seemed to be more optimistic as to the prognosis of postgastrectomy gastritis than Schindler has been. They have suggested the use of dietotherapy of the ambulatory ulcer type

in the treatment of anemia. These observers have suggested the use of gastric lavage and noted the surprising fact that patient with achlorhydria seemingly were made worse by the administration of hydrochloric acid by mouth and were relieved by the administration of an alkali.

In 1930 Moutser and Ghelew reported the results obtained by gastroscopic examination of 143 patients who previously had undergone operations on the stomach. The following operations had been performed: gastro-enterostomy in 96 cases, partial gastrectomy in 32 cases, operation for a perforated ulcer in 14 cases, gastropasty in 2 cases and excision of an ulcer in 1 case. In 6 of the 33 cases in which partial gastrectomy or excision of an ulcer had been performed, anterior gastro-enterostomy had been performed previously. In 1 of the 33 cases, the ulcer had been cured. The following types of partial gastrectomy had been performed in the remaining 32 cases: the Péan-Billroth (Billroth I) operation in 2 cases, the Billroth II operation in 4 cases, the Polya operation in 13 cases, the Finsterlin operation in 6

cases, Finsterer a pyloric exclusion combined with partial gastrectomy in 4 cases, and Finney a (Billroth I) in 1 case

Resection for carcinoma was not performed in any case in this series These observers found persistent old ulcers, new ulcers ulcerative gastritis, severe gastrojejunitis, stomal edema, and more or less important atrophy almost as frequently in cases in which gastroenterostomy had been performed as they did in cases in which partial gastrectomy had been performed In their opinion what could be called a normal gastroscopic appearance was observed in few if any of the cases The gastroscopic findings ranged from mild atrophy to severe ulceration and hypertrophy

Minnakata in 1930 reported the results of an experimental study of gastritis which occurred after gastric resection He performed a Billroth II operation on 13 dogs In each instance, he performed a wide excision of the antrum and the pylorus The dogs were observed for from one to twelve months after the operation was performed Atrophic degenerative changes were the only lesions observed on the gastric side of the anastomosis In 54 per cent of the dogs, inflammatory changes occurred on the jejunal side of the anastomosis The remaining portion of the stomach showed signs of gastritis in the shortened, stiff mucosal folds and in the pleriform layers of the

Christiansen in 1943 reported on the gastroscopic examination of 10 patients who had undergone gastric resection He found that only 1 of the 10 patients had a normal gastric mucosa In the other 9 cases the examination disclosed superficial, hypertrophic, atrophic, erosive or ulcerating elements, mostly localized to the stoma and adjacent intestine He said that postoperative gastritis may develop even if the stoma is contracted or if free hydrochloric acid is absent Morphologically the postoperative gastritis appeared to him to be a special form of gastritis In cases in which objective improvement was observed, only the superficial erosive or ulcerative elements were present, while the hypertrophic and atrophic elements seemed incurable He agreed with Schindler that the prognosis was grave and he said that there seemed to be no satisfactory treatment and that repeated resection did not control the pathologic process

One of us (W C M) recently stressed the point that gastritis microscopically is an extremely difficult entity to classify and that it probably should be considered as a single process It begins with a

common or a set of common etiologic factors which will produce the immediate acute inflammatory reaction of acute gastritis. If the etiologic factors are removed the stomach slowly will return to normal. If these factors continue to affect the gastric mucosa a variable picture will be seen microscopically and gastroscopically (depending on the factors of the severity of the underlying cause, the length of time it has been present and the amount of repair the organism as a whole is able to muster) and a state of chronic gastritis will occur. It is suggested that the chronically deplussed patient with ulcer is unable to muster the resistance and the nutritive building blocks necessary to repair the damage of an antecedent gastritis or to resist the new inflammatory process initiated by the sudden change in gastric function caused by partial gastrectomy.

Wollaege, Comfort, Weir and Osterberg in 1940 studied the total solids, fat and nitrogen in the feces of 14 patients who had undergone partial gastrectomy and anastomosis of the entire cut end of the stomach to the jejunum. They found that nearly all of the patients lost more fat in the stools when they were taking a high fat diet than did a series of controls. This loss occurred in patients who did not complain of any symptoms referable to the digestive tract, but it tended to be greater among the patients who had postoperative digestive symptoms (not associated with recurring peptic ulceration). Some of the group also lost more nitrogen and total solids in the stools than did persons who had not undergone an operation on the stomach. These authors said that, unless a diet of sufficient caloric content to compensate for the loss was given a decrease in body weight might be expected.

In an attempt to obtain further information on this problem, we have taken at random 25 cases in which the patients underwent partial gastrectomy at the Clinic and returned at a later date because of symptoms which were referable to the stomach and of such severity that gastroscopy was warranted. This group of patients represents approximately 25 per cent of the total number of patients on whom gastrectomy was performed for any reason after a previous partial gastrectomy since 1935. The group was studied with especial regard to duration of time since partial gastrectomy, the type of operative procedure performed, the pathologic changes that were present at the time of operation, the presence or absence of free hydrochloric acid in the remnant of the stomach, the roentgenologic findings, and the appearance of the gastric mucous membrane as reported by the gastroscopist. It was found that the result of the operation could not

be said to have been satisfactory in any of these cases. The gastric symptoms disappeared temporarily but they always recurred. They eventually became severe enough to warrant gastroscopy.

The time which had elapsed between partial gastrectomy and gastroscopy was as follows: less than one year in 6 cases, one year in 3 cases, two to four years in 11 cases and four to nine years in 3 cases.

The following operative procedures had been performed in this series of cases: posterior Polya operation in 12 cases, disconnection of gastro-enteric anastomosis and posterior Polya operation in 9 cases, von Haberer's modification of the Billroth I operation and closure of the openings created in the stomach and duodenum by a gastroduodenostomy in 1 case, von Haberer's operation and disconnection of a gastro-enteric anastomosis in 1 case, Moynihan's modification of the anterior Polya operation in 1 case, and Hoffmeister's modification of the anterior Polya operation in 1 case.

Partial gastrectomy had been performed for the following pathologic conditions: duodenal ulcer in 15 cases, gastrojejunitis in 4 cases, gastrojejunal ulcer in 2 cases, chronic gastritis and a duodenal ulcer in 1 case, chronic erosive gastritis in 1 case, tuberculosis of the stomach in 1 case, and gastritis and malfunction of a reconstructed pylorus in 1 case. The presence of superficial, erosive, ulcerative, atrophic and hypertrophic forms of gastritis was confirmed microscopically in all cases. The microscopic criteria for the diagnosis of gastritis were those outlined by Jack¹ and now commonly accepted as bona fide evidence of gastritis. Briefly they are: (1) destruction of chief and parietal cells, (2) replacement of the gastric mucous membrane by mucous cells in severe forms of gastritis the replacement produces an "intestinalization" so to speak, of the mucous membrane of the stomach and often results in the formation of cysts, (3) thickening and fibrosis of the muscularis mucosae, which often leads to alterations in the gastric folds, and (4) infiltration of the mucosa by lymphocytes and plasma cells.

Achlorhydria was a constant finding preoperatively and no free acid was found in the gastric contents.

Roentgenologic examination was performed in all cases. In 20 of the cases the findings were called normal by the roentgenologists. In 2 cases a diagnosis of gastrojejunitis was made on the basis of slight narrowing of the stoma. In 2 cases a diagnosis of stomal ulcer was made and in 1 case a diagnosis of gastritis was made on the basis of hypertrophic folding of the mucosa.

The following diagnoses were made gastroscopically: gastrojejunal

ulcer in 5 cases, gastrojejunitis in 8 cases, postoperative gastritis in 10 cases, a normal but atonic stomach in 1 case and an indeterminate lesion in 1 case.

SUMMARY AND COMMENT

This paper is based on a study of 25 patients, taken at random, who had undergone gastric resection and who returned to the Clinic for further study because of persistent symptoms referable to the gastro-intestinal tract. The duration of symptoms after partial gastrectomy for a variety of inflammatory conditions of the stomach and duodenum appears to be important only in so far as the findings in this group of cases illustrate the early appearance of symptoms post-operatively and the tendency for the occurrence of periods of improvement followed by periods of severe exacerbation. In the average case of postgastrectomy gastritis nutrition is impaired and the patient frequently seeks medical relief.

It is not within the scope of this paper to consider the relative merits of the various methods of restoring gastro-intestinal continuity after resection of the stomach, but it may be pointed out that during the period covered by this study the Polya operation has been the procedure of choice when partial gastrectomy has been required. The fact that postoperative gastritis may follow any type of gastro-enteric anastomosis is well known, and if the records were available and carefully examined it would be found probably that no one type of anastomosis is particularly likely to cause gastritis.

The pathologic condition for which most of the resections were performed was duodenal ulcer; this was the indication for the operation in 60 per cent of the cases. In 24 per cent of the cases, the operation was performed because a previous gastro-enterostomy had caused such complications as gastrojejunitis and gastrojejunal ulcer. In the remaining cases, the resection was performed for miscellaneous reasons such as chronic erosive gastritis, tuberculosis of the stomach, and malfunction of a reconstructed pylorus. Microscopic examination disclosed coexistent gastritis in all of the 25 cases. This would seem to indicate that a part, at least, of the gastritis found at later gastroscopy in this group of cases was a persistence of a pre-existing lesion. That gastritis of equal degree may have been present preoperatively in the very large number of patients who obtained a satisfactory result after partial gastrectomy is admitted and further study along this line is in progress at present. Irrespective of this possibility it would seem evi-

dent that even greater emphasis should be placed on the necessity of rigid postoperative management in those cases in which microscopic examination discloses evidence of extensive gastritis at the time partial gastrectomy is performed. Routine microscopic examination of the specimens should be made in all cases and special interest should be focused on the mucosa in the proximal portions of the excised tissue in order to demonstrate as accurately as possible the presence or absence of residual gastritis in the remnant of stomach that has been preserved.

Röntgenologic examination is admittedly of little or no value in attempting to determine the presence or absence of gastritis after a partial gastrectomy has been performed. The most that can be expected of the roentgenologist is some statement as to the patency of the gastro-enteric stoma and perhaps a theoretical conjecture as to the role that edema may play in producing a deformity of the stoma. An ulcer can be visualized with reasonable accuracy but a roentgenologic diagnosis of gastrojejunitis, gastritis or even stomal edema has apparently been inaccurate and undependable.

Gastroscopic examination revealed a normal stomach in 1 case and an indeterminate lesion in another case. In the remaining 23 cases gastroscopic examination disclosed postoperative gastritis or gastrojejunitis of sufficient severity to account for the distressing symptoms.

Response to adequate therapy in these cases has been slow and discouraging but we are inclined to agree with Browne and McHardy¹ that the problem is not entirely hopeless. Reassurance, encouragement and an adjustment in the patient's mode of living so that adequate rest and relaxation may be obtained and physical and nervous fatigue may be avoided can accomplish a great deal if combined with proper diet and medication. A similar regimen should be formulated for all patients who undergo partial gastrectomy if the full benefits of this operation are to be realized.

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TRAUMATIC PARALYSIS OF THE SCIATIC NERVE ASSOCIATED WITH FRACTURE OF THE RIM OF THE ACETABULUM AND DISLOCATION OF THE HIP

HENRY W. MEYERDING

THE successful treatment of severe injuries from accidents in this age of rapid transportation requires expert medical and surgical care. A rare combination of injuries involving the hip is traumatic sciatic paralysis with fracture dislocation of the acetabular rim and dislocation of the hip.

This type of injury usually occurs while the patient is in a sitting position and is thrown against the dashboard of a car so that the force is carried through the femur and the head of the femur is driven through the posterior rim of the acetabulum. Two types of injury to the nerve may result, the primary and the secondary. The fractured fragment may be carried upward toward the sciatic notch and the nerve may be torn, stretched or even completely severed immediately producing a primary neuritis. Secondary type of nerve injury may occur some weeks after the injury to the bone and usually is the result of hematoma, scarring or callus or of all three. These produce pressure and eventually paralysis.

After a fracture of the rim of the acetabulum and dislocation of the hip it is extremely important that the attending physician examine the patient immediately for evidences of traumatic neuritis. In order to obtain the best result in the treatment of a nerve injury of this type, prompt surgical intervention should be instituted in order to prevent irreparable damage with permanent disability.

The dislocation of the hip should be reduced and the fragment of bone replaced or removed to relieve the pressure from the nerve and end to-end anastomosis of the sciatic nerve should be performed if

90 degrees and the foot is held at right angles. This position relieves tension on the damaged nerve and also permits the patient to change his position frequently. The latter prevents bed-sores. The cast may be removed in two to three months and physical therapy started. If foot drop persists the patient should wear a support, such as a right-angle catch brace or a molded padded plaster splint.

When a period of months has elapsed since the injury and scar tissue and contracture have developed it is extremely difficult to reduce the dislocation by manual manipulation or even by surgical measures. It may be necessary to resort to heavy skeletal traction as illustrated by case 1 which is reported in detail in this paper. Surgical treatment likewise may fail to give relief in this secondary type of nerve injury. Under such circumstances conservative measures such as physical therapy and application of braces for foot-drop for a prolonged period must be instituted but the prognosis is doubtful.



Fig. 254 (Case 1).—Bilateral comminuted fractures of the rims of the acetabula one day after accident, left hip, fracture of the posterior rim of the acetabulum: (1) upward and outward displacement of the fragment and posterior dislocation of the head of the femur; right hip, comminuted fractures of the acetabulum.

The common complications in this type of injury are (1) trophic ulcer (2) foot-drop, (3) aseptic necrosis (4) traumatic arthritis or (5) a combination of these.

Both hips may be affected with or without paralysis of the sciatic nerve (Fig. 254).

REPORT OF CASES

CASE 1.—The injury occurred when the patient, man aged 42 years, drove his automobile into a tree and sustained fractures of both hips and traumatic sciatic paralysis on the right side only (Fig. 254).

CASE 2—Fracture of the Rim of the Left Acetabulum with Dislocation of the Head of the Femur. Traumatic Sciatic Paralysis and Foot drop.—A man, 30 years of age, was admitted to the Clinic August 31, 1944. He gave a history of having fallen asleep while driving an automobile and of sustaining injury to the left hip ten weeks prior to his admission. He stated that he had been treated for fifteen days by means of 15 pounds (6.8 kg.) of skin traction to the

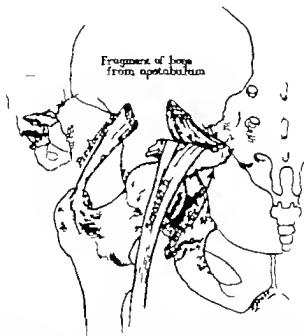


Fig. 285 (C & G).—At operation posterior dislocation of the hip and fracture of the left acetabulum were found with fragments displaced backward and upward. The component of the sciatic nerve was stretched over the sharp edge of the displaced fragment.

left leg, then a pin was inserted through the distal end of the femur and skeletal traction of 16 pounds (7.3 kg.) was applied for six weeks. The wounds of the pins became infected and the pin was removed two weeks prior to his admission to the Clinic. He then had been up on crutches but said the deformity and pain in the hip and inability to dorsiflex his left foot had not

mercury and the diastolic 68 mm. The pulse rate was 80 beats per minute and the temperature was normal. The patient was a well-developed white man who was apparently disabled and in pain as he lay in bed, the left leg was partially flexed and internally rotated with visible shortening. There were two holes in the skin above the left knee; pus was draining from the medial one. Tender ness over the course of the left sciatic nerve and greater trochanter and peroneal palsy and foot-drop were noted. There were recent scars of the face and arms. The roentgenograms of the left hip showed upward and posterior dislocation of the left femoral head and a large fragment of bone compressing the posterior wall of the acetabulum which had been fractured and dislocated backward and upward with several small bony fragments.

Exploration of the sciatic nerve, reduction of the dislocation of the hip and removal of the fragments of bone were advised by the neurosurgical and orthopedic consultants. Operation was performed September 8, 1944 at which time a posterior oblique incision was made over the left hip and a large fragment of bone was found displaced upward with the sciatic nerve stretched over the top (Fig. 663). The outer branch showed marked atrophy resulting from pressure; the next root lay over a sharp eminence which was almost knife-like. The displaced fragment was removed; this procedure relieved the nerve. The fragment measured 1½ inches (3.8 cm.) in width and 1 inch (2.5 cm.) in thickness. The head of the femur was visible and was caught in dense scar tissue which was excised but the femoral head could not be returned to position even when great force was employed together with loose skin. It was deemed inadvisable to continue further surgical procedure at this time and the patient was returned to bed. After another unsuccessful manipulation, skeletal traction of 33 pounds (15.0 kg.) was applied seven days later by means of a Kirschner wire passed through the upper end of the tibia. The operative wound on the hip healed with primary intention. Three weeks after traction was started, the patient experienced a snapping sensation and found that he could externally rotate the leg and had less pain. Roentgenographic examination showed the head of the femur in the acetabulum; the Kirschner wire was removed and plaster of paris spica cast which extended from the hip to the toes was applied. The patient was discharged from the hospital ten and a half months after admission.

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The patient returned for observation about one year after operation, at which time examination revealed satisfactory progress and the roentgeno-

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COMMENT

Two rare instances in which the patients had traumatic sciatic paralysis complicating fracture of the acetabulum with posterior dislocation of the hip form the basis for this presentation. The case of one patient was presented in detail. The patients were seen several months after the injury and at that time treatment of the paralysis, dislocation and scar tissue presented a complicated problem. I believe that immediate evacuation of hematoma, reduction of the dislocation of the hip, removal or replacement of the fragment and repair of the nerve when severed are indicated in order to obtain the best results.

GANGRENOUS CHOLECYSTITIS A CLINICAL AND PATHOLOGIC STUDY OF 100 CASES*

LEONARD C. HALLENDORF MALCOLM B. DOCKERTY
AND JOHN M. WAUGH

THE pathology of gallbladder disease and its clinical application have been a never-ending source of interest to clinician and to surgeon alike for many years. Pathogenetically controversial, cholecystitis is frequently associated with gangrene and yet there seemed to be no detailed clinical and pathologic appraisal of a large series of cases of gangrene of the gallbladder. This then is the reason for the present study.

HISTORICAL

Gangrenous cholecystitis is by no means a recent clinical entity for Hotchkiss reported the first case in which operation was performed in 1894.¹ Interestingly enough, W. J. Mayo removed entirely a gangrenous gallbladder in 1899 at a time when even the more courageous surgeons were still doing cholecystostomy for all forms of gallbladder disease. For a classic description of a surgical case one should refer to that reported by Gibbon in 1902.²

REVIEW OF LITERATURE

With an incidence of 1 to 3 per cent of all surgical cases of cholecystic disease and 25 to 35 per cent of acute cases, gangrenous cholecystitis commonly occurs in an older age group than other forms of cholecystitis.^{3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100} Maier explained this by stating that gallbladders in older people are less distensible and less vascular because of varying degrees of arteriosclerosis present, thus encouraging circulatory disturbances and gangrene.

As a rule symptoms were observed to be severe although many report stated that there was no correlation between the clinical picture and the pathologic state. Disagreeing with this Samt²⁴ said that the most important single clinical manifestation was the development of a tender palpable gallbladder indicating a progressive obstructive process. This could cause distention to a dangerous degree and lead to gangrene and perforation because the retained fluid could not escape.

*Abridgment of thesis submitted by Dr. Hallendorf to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

by the obstructed cystic duct. Progressively worsening of the patient naturally occurred with the unrelieved obstructive process.

Most reports agreed that gallstones were almost always present in cases of gangrene. Numerous investigators demonstrated the high incidence of obstruction of the cystic duct by one or more gallstones. Excellent studies by Feinblatt, Andrews, and Denton showed that the basic lesion in gangrenous cholecystitis was vascular damage occurring after acute obstruction. They found edema, hemorrhage, congestion and necrosis in varying degrees, depending on the duration of the obstruction. Vest and others⁴ expressed the belief that infection was the basic lesion and yet several investigators found a high percentage of acute cases to be sterile on culture and Andrews found that the "purulent fluid" in so-called empyema of the gallbladder was not pus at all. It was really precipitated calcium or cholesterol.

Significantly, Hornans said that if gangrene were due primarily to bacterial rather than to circulatory causes, acute cholecystitis would be an even more dangerous disease than it was and operation would spread rather than restrain infection, whereas early operation at what might seem to be a most violent stage of infection was followed by rapid healing.

The analogy to gangrenous appendicitis was obvious. From the excellent work of McCallig on appendicular obstruction, it was rary to see that the fecolith in the appendix had as its counterpart in the gall bladder the stone obstructing the cystic duct. Gangrenous appendicitis was generally more lethal than gangrenous cholecystitis, for the appendix was usually teeming with organisms, while the gallbladder

obstruction better than the appendix.

More and more surgeons were looking on gangrenous cholecystitis as they did on gangrenous appendicitis. " " " " they concluded that the procedure of choice was to remove the offending organ completely at the earliest opportunity.

MATERIALS AND METHODS OF STUDY

In order to obtain 100 cases with complete clinical records and

had elapsed since the last attack before surgical exploration and on the appearance of structures at operation.

Early in the investigation we learned to search the edematous and distorted gallbladder carefully for the cystic duct and to ductect it out completely for our clinical abstracts indicated that stones impacted in the region of the cystic duct would appear frequently. We were rewarded in this search, for in a number of cases we found impacted gallstones that had been overlooked by the surgeon or the pathologist on the day of the operation.

Careful microscopic inspection was then made of three sections cut from each gallbladder and stained with hematoxylin and eosin: one from the region of the cystic duct, one from the wall of the midportion and one from the fundus of the gallbladder.

INCIDENCE

Gangrenous cholecystitis occurred in approximately 2.5 per cent of all patients coming to surgical exploration for cholecystic disease at the Clinic, while in surgical cases of acute cholecystitis, it made up about 33 per cent. Males and females were affected about equally. The average age of patients was 58 years, while 37 per cent were more than 50 years of age.

CLINICAL PICTURE

In 75 per cent of cases symptoms were typical of recurrent acute cholecystitis and of chronic cholecystitis. In only 12 cases was there only one attack. Jaundice occurred in only 12 cases.

Atypical location and unusual severity of the pain occasionally led to a diagnosis of coronary occlusion, acute appendicitis or perforated peptic ulcer. Treacherous disappearance of pain while other clinical evidence indicated progression of the pathologic process occurred in several cases, presumably coincident with the onset of gangrene, as observed by Saint²².

Significantly a palpable tender gallbladder was present in 39 cases. This brownish-red, firm, globular mass was

As Saint²²:

"... as the onset of an attack of acute obstructive cholecystitis, this palpable gallbladder was globular and cystic in character—a definitely distended viscus. Later

after the omentum and the neighboring structures tended to wall off the acutely inflamed organ the contour became that of a firm, irregular mass and was less characteristic of the gallbladder. It was not unusual for a greatly distended gallbladder to be felt as far down as the umbilicus or below. In one instance in which symptoms pointed to the right lower abdominal quadrant and in which the greatly distended gangrenous gallbladder wallled off with omentum, was palpated below



Fig. 206.—Distended, enlarged, gangrenous gallbladder that was palpable in the lower right region of the abdomen and that was thought to be an appendiceal abscess.

the umbilicus, the operative diagnosis was retrocecal appendiceal abscess (Fig. 206).

DIAGNOSIS

Naturally gangrenous cholecystitis was clinically diagnosed very infrequently for clinicians and surgeons alike did not distinguish cases of gangrenous cholecystitis from others considered acute just as is commonly done in acute appendicitis. Chronic cholecystitis was the clinical impression in about one half of the cases.

Gangrenous cholecystitis should always be suspected if the patient is more than 50 years of age if there is a history of repeated biliary colics and dyspepsia in the past few years if the recent attacks were much more severe than past ones if the attack lasts more than a few hours and seems to be progressing as indicated by the rising pulse rate and increasing temperature and the general debility of the patient and if there is a palpable tender gallbladder with or without abdominal rigidity



Fig. 287.—Greatly enlarged, tense, distended, gangrenous gallbladder contrasted with normal sized one. The larger specimen measured 24 cm. in length.

GROSS PATHOLOGY

Gallstones.—In 88 of the 100 gallbladders studied, gallstones were

by 4 by 4 cm. Most of the specimens measured at least 10 by 3 by 3 cm. As a rule the walls were greatly thickened, varying from a "normal" thickness of 1 mm. to the maximum of 30 mm., the average being 6 to 9 mm.

Shape and Character.—Most of the specimens were elongated and cylindrical, resembling to some degree a large sausage with fairly stiff rubbery walls. The lower or cystic duct end was almost of the same diameter as that of the fundus because of the obstruction of the cystic duct so commonly present. The cystic duct itself was frequently

hard to find because of the gross distortion and edema present. Commonly it was elongated and tortuous, folded on itself and adherent to the serosal aspect of the gallbladder. The mucosa was commonly black and discolored, friable, ulcerated and partially desquamated. An enlarged firm cystic lymph node was found attached to the gallbladder in the region of the cystic duct in about one half of the cases.



Fig. 206.—*Specimens as in Figure 207 opened. There is a stone measuring 1 cm. in diameter in the cystic duct in the larger specimen, which is not directed out in this photograph.*

In one unusual case, the destruction was so great that the mucosal layer had completely separated from the outer coats of the gallbladder thus forming two complete separate sacs (Fig. 200).

Contents.—Usually the fluid found in the gallbladders was cloudy and dark. Frequently it was hardly recognizable as bile and occasionally it was frankly purulent. Unfortunately cultures were done in only 26 cases, in 10 of which the fluid was sterile. Of the 7 positive cultures, gram-negative bacilli were found in 4 cases, streptococci were found in 2 cases and yeast organism were found in 1 case.

Perforation.—Perforation of the gallbladder occurred in 24 cases, usually at the fundus and commonly was walled off by the omentum,

the duodenum or the edge of the liver. In 9 cases the rupture had occurred onto the under surface of the liver forming small abscesses or pockets of stones in the hepatic substance. Cholecystochole and cholecystoduodenal fistulas each occurred once. Acute free perforation did not occur in our series of cases, as contrasted with the experience



Fig 268—Severe destruction in gangrenous gallbladder with complete separation of mucosal sac from the outer coats of the gallbladder. The mucosal sac is hanging free, attached only by the cystic duct.

of Conley and Harkins, who found that one fourth of their series of 25 consecutive perforations were of the free type.

OBSTRUCTION OF THE CYSTIC DUCT

Obstruction of the cystic duct was present in 63 cases. In 59 of these cases, the obstruction was due to one or more gallstones tightly impacted in the duct or in the region of the duct (Fig. 270). In some cases the obstructing stone was too large to enter the cystic duct itself but

nevertheless it was firmly impacted in the neck or lower end of the gallbladder. In many cases there was dilatation of the duct, with the stone that had apparently caused the dilatation after repeated colics firmly lodged in the very proximal end of the duct. The duct was occasionally distorted and tortuous and it required careful dissection to lay it open entirely.



Fig. 278.—Multiple gallstones in gangrenous gallbladder, with one stone impacted in the cystic duct.

The operating surgeon had actually felt the stone obstructing the duct in 44 cases, while in another 12 cases the pathologist had discovered the stone. Both surgeon and pathologist had found the stone in 10 cases, while in the last group of 23 cases we found adherent, impacted gallstones or stony fragments, and ulcerated regions or pockets where a stone had been lodged that had been overlooked by both surgeon and pathologist. It must be remembered that cholecys-

tectomy in the presence of the extensive edema and distortion associated with the gangrenous process was very difficult and frequently any stone in the cystic duct was dislodged by the surgeon in isolating and clamping the duct.

MICROSCOPIC PATHOLOGY

Histologic evidence seemed to indicate that circulatory disturbances played the biggest role in the pathogenesis of gangrenous cholecystitis. However, evidence of infection in an appreciable number of cases could not be disregarded although it usually appeared late. Generally pathologic changes were most severe in the region of the fundus and

TABLE 1
SUMMARY OF MICROSCOPIC FINDINGS IN 100 CASES

Histologic Feature	Cases
Edema	84
Necrosis	100
Hemorrhage	91
Hypertonia	97
Thrombosis	23
Lymphocytes	90
Polymorphonuclear cells	61
Giant cells	10
Plasma cells	9
Fibroblasts or fibrosis	93
Submucosal edema of arteries	73
Relatively Aschoff nodules	79

in the submucosal stratum of the wall of the gallbladder. Table 1 gives a summary of the histologic features found in our specimens.

Necrosis.—There was extensive necrosis in all of the cases, so extensive in some that it resembled complete infarction (Fig. 871). For the most part, these infarcted regions involved the mucosa and the tissues immediately adjacent to the mucosa. Usually the entire section being studied was involved and the wall of the gallbladder had a characteristic, pale pink, "ghostlike" appearance. Although massive necrosis commonly occurred in the midportion of the wall, it was less frequently seen in the stratum near the peritoneal surface of the gallbladder. Necrosis was usually more extensive in the fundic portions of the viscus than in other portions.

Edema.—Intramural edema was observed fairly constantly. It seemed to occur early in the obstructive process for it was more

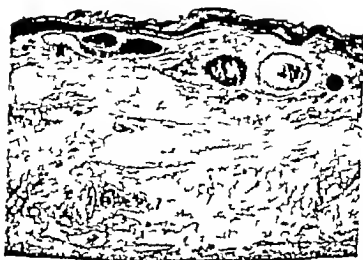


Fig. 871—Extensive necrosis revealing complete infarction in gangrenous gallbladder especially in the mucosal region. Note the marked congestion and moderate edema. The muscle stratum is discernible though necrotic. This is an early case (hematoxylin and eosin $\times 13$).

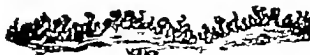


Fig. 872—Cross section of gallbladder with minimal pathological change. Contrast this with Figures 873. Both magnified the same (hematoxylin and eosin $\times 13$).

severe and more extensive in the acute fulminant type case in which surgical exploration was performed shortly after the onset of the illness than in cases in which operation was performed later. Much of the thickness of the wall in these cases was due to edema as con-

trasted to the extensive fibrosis in the older cases (Figs 878 and 879). Edema tended to disappear as the process grew older.

Venous Congestion.—In 50 cases venous congestion was present. It was more severe in the early than in the later cases. Frequently the vessels were so packed with erythrocytes that it was difficult to distinguish congestion from actual thrombosis (Fig 871). Interestingly congestion seemed to occur in the serosal vessels in the older cases.



Fig 878.—Early case of gangrenous cholecystitis with extensive, severe edema. Note also the submucosal hemorrhage, the destruction of serosa and the extensive necrosis (hemostasy and areas $\times 10$).

Hemorrhage.—Intramural hemorrhage of some degree was present in 91 of the specimens. It was seen in all of the various strata of the wall, but seemed to be most common in the submucosal region. In a number of cases, there was a peculiar stratum of hemorrhage just beneath the peritoneal surface of the gallbladder (Fig 874). This could well represent a hemorrhagic ring that extended all of the way around the gallbladder. In some regions rupture of the vessel could be

seen with erythrocytes migrating out into the interstitial tissues. Perineural and perivascular hemorrhage occurred occasionally.

In older cases fragmentation and distortion of erythrocytes were seen. Brown pigment granules, probably derived from degeneration of erythrocytes in a hemorrhagic region, were commonly present.

Thrombosis.—Definite venous thrombosis occurred in 25 cases. In the early cases of course the thrombus was fresh and readily identifiable (Fig. 275). These borderline thromboses which resembled hyperemic vessels were excluded from the tabulation. In several older cases thrombi were seen in which organization and canalization



Fig. 275.—Extensive subepithelial hemorrhage in gangrenous gallbladder. Adjacent fibroblastic proliferation. Pericholangitis (granulation) in wall (case X200).

had taken place. In these cases fibroblastic repair was going on at the same time in neighbouring tissues.

Mucosal Changes.—In practically all of the cases there was some mucosal desquamation and in the more severe cases the mucous membrane was completely destroyed. When present, it was flattened by the distending fluid in the gallbladder. Only occasionally were villi seen and these were usually in the region of the cystic duct, where minimal pathologic changes occurred *anyway*, if any were present. Epithelial cells were necrotic, shrunken, distorted and fragmented. Occasionally vacuoles could be seen in a mass of cells. The epithelial

cells were occasionally extensively necrotic, especially in those cases in which the lesion resembled infarction in which the entire wall in the region studied was a solid sheet of necrosis.

The infoldings of epithelium commonly called Rokutansky Aschoff sinuses were seen in 20 cases. We considered them as an incidental finding although Glenn and Moore suggested that they might become walled off form an abscess and eventually result in perforation.

Arterial Changes.—An interesting and peculiar feature of the arteries in 23 cases in our series was subintimal edema and proliferation in an otherwise normal arterial vessel. Frequently this process almost completely occluded the lumen of the vessel (Fig. 275).



Fig. 275.—Early recent thrombus in lumen of gangrenous gallbladder. Adjacent cellular infiltration (hematoxylin and eosin $\times 100$).

Whether this phenomenon was part of the general picture of edema also reflected in the perineural edema present, or whether it was an attempt to repair the damaged vessel was a matter of speculation. Its appearance in older cases suggested that it was a reparative process. It was a possible factor in arterial obstruction added to that already present from the passive congestion and edema resulting from the original obstruction of the cystic duct.

Proliferation of Fibroblasts.—Fibroblastic activity in some stage was present in practically all of the cases except the very early ones. This undoubtedly represented attempts at repair of the injured

tissues. Fibroblasts presumably were laid down over several days time on the fibrin network in the edematous, hemorrhagic walls resulting from the initial circulatory disturbance. Fibroblasts of all ages were seen from the large immature closely-grouped spindle cells without collagen seen in the early acute cases to the dense fibrosis with relatively few cells and with extensive hyalinization of the collagen seen in the very old cases. In many of these older cases, the wall of the gallbladder was one solid sheet of fibrous, with no recognizable muscle or mucosa present (Fig. 477).



Fig. 478.—Substantial edema and proliferation in an artery of pancreas guinea pig bladder. Note the marked occlusion of the lumen (hematoxylin and eosin $\times 133$).

Cellular Infiltration.—Lymphocytic infiltration was almost invariably seen, especially in the early cases, apparently a relic of a previous inflammatory process. Pericholecystitis, characterized by lymphocytic infiltration of the peritoneal surface of the gallbladder was found in about one half of the cases.

Polymorphonuclear cells almost invariably did not appear for several days after the acute onset occurred. Their presence could not be minimized, for frequently they occurred in large numbers and they were present in 41 cases of the series. Micro-abscesses were not uncommon. The late appearance of these cells implied that infection

occurred secondary after the tissues had already been severely damaged.

In some of the older cases about 10 per cent of the 100 cases studied foam cells, plasma cells and multinucleated giant cells were seen probably representing reaction to long-standing inflammation and necrosis.

Bile Pigment.—Bile pigment in some degree was present in practically all of the cases. The bright, golden yellow color of the pigment particles and crystals was generally characteristic. Usually these



Fig. 277.—Old case. 24th extensive fibrosis and healing in gangrenous gallbladder (hematoxylin and eosin, X125).

particles were scattered throughout the wall of the gallbladder. Occasionally a layer of apparently desiccated bile pigment was found covering the epithelium of the internal surface of the gallbladder.

In one remarkable case there was so much bile pigment present that it could be seen in the tissue section without the aid of the microscope. Macroscopically large particles and crystals could be seen scattered throughout the wall of the gallbladder.

masses of the pigment
amounts, particularly in

phenomenon resulted from bile penetrating into the wall of the gallbladder from the liver through a wide area of perforation and fistula formation into the liver that was present in this neglected long-standing case.

Presence of bile pigment in the wall of the gallbladder recalled the experimental work of Womack and Bricker who tied off the cystic ducts in dogs, injected saline solution and various concentrations of bile into the gallbladders and later examined the specimens. They found that replacement of the normal bile with salt solution in the obstructed gallbladder produced minimal lesions while injection of concentrated dog bile produced violent hemorrhagic, gangrenous lesions.

PATHOGENESIS

In this series of 100 cases there was enough difference in duration of time from onset to operation so that a representative sequence of histopathologic happenings could be described from one day up to several weeks. As clearly as was possible we dated the pathologic age of the recent changes from the onset of the last attack of biliary colic prior to surgical exploration. Since in most of the cases symptoms developed from impaction of a stone in the cystic duct with resultant increase of tension within the gallbladder and circulatory disturbance, and since in many cases there was a history of repeated attacks of colic, it must be remembered that a mixed picture could be produced. For in a gallbladder that had experienced several episodes of obstruction in the past the new acute process was superimposed on any stage of recovery or progression from the previous attack that was present. However choice of cases in which attacks before the one leading to operation had been mild or absent gave us a fairly representative picture of what happened from day to day.

First Day—In cases in which operation was done within the first twenty-four hours after the onset of an attack, extensive edema and marked venous congestion were characteristic. There was moderate intramural hemorrhage and fairly extensive lymphocytic infiltration. Fibroblastic activity was absent or minimal while extensive necrosis and mucosal desquamation were common. Polymorphonuclear cell were rare or completely absent.

Second Day—Fairly extensive edema and marked congestion
 ————— necrosis occurred mainly in

fibroblasts were seen. Congestion seemed to remain unchanged while pericholecystitis made its appearance. Extensive necrosis was still present while polymorphonuclear cells increased.

Fourth Day—For the first time subintimal edema of the arteries was present although it more commonly occurred later. Moderate edema persisted while hemorrhage was more extensive. Polymorphonuclear cells were numerous, more fibroblastic activity was present and bile pigment was frequently seen.

Seventh Day—Edema and congestion were minimal while thrombosis was occasionally seen. Hemorrhage was moderate and subperitoneal hemorrhage began to appear. There was moderate fibroblastic activity with beginning formation of collagen. Infiltration of

TABLE 2
SUMMARY OF POSTOPERATIVE COMPLICATIONS IN 100 CASES

Complication	Cases
Wound infection	3
Wound dehiscence	4
Prolonged fever	3
Postoperative pneumonia	1
Postoperative telecystitis	1
Vascular pulmonary embolism	1
Acute femoral thrombophlebitis	2
Delayed bronchobiliary fistula	1
Acute urinary retention	1
Adhesions	1
Postoperative hemorrhage from the incision	1
Peritonitis	2

polymorphonuclear cells was extensive now and subintimal edema of the arteries was more frequently seen.

Eleventh Day—Edema was almost entirely absent now and there was moderate fibrosis. Polymorphonuclear cells were in great profusion now and macro-abscesses were common. Venous thrombi were common. Bile and blood pigment were commonly found while sub-

was frequently replaced by massive fibrosis. Subperitoneal hemorrhage persisted and subintimal arterial edema was common.

Thirtieth Day—Extensive fibrosis was still evident, indicating a fairly complete state of repair. Cellular infiltration was almost entirely

phenomenon resulted from bile penetrating into the wall of the gallbladder from the liver through a wide area of perforation and fistula formation into the liver that was present in this neglected long-standing case.

Presence of bile pigment in the wall of the gallbladder recalled the experimental work of Womack and Bricker who tied off the cystic ducts in dogs, injected saline solution and various concentrations of bile into the gallbladders and later examined the specimens. They found that replacement of the normal bile with salt solution in the obstructed gallbladder produced minimal lesions, while injection of concentrated dog bile produced violent, hemorrhagic, gangrenous lesions.

PATHOGENESIS

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Second Day—Fairly extensive edema and marked congestion persisted. Moderate and more severe hemorrhage occurred mainly in the submucosal stratum. Mucosal desquamation was severe.

Third Day—Edema had subsided somewhat and more young

Fibroblasts were seen. Congestion seemed to remain unchanged while pericolecystitis made its appearance. Extensive necrosis was still present while polymorphonuclear cells increased.

Fourth Day—For the first time subintimal edema of the arteries was present, although it more commonly occurred later. Moderate edema persisted while hemorrhage was more extensive. Polymorphonuclear cells were numerous, more fibroblastic activity was present and bile pigment was frequently seen.

Seventh Day—Edema and congestion were minimal while thrombosis was occasionally seen. Hemorrhage was moderate and subperitoneal hemorrhage began to appear. There was moderate fibroblastic activity with beginning formation of collagen. Infiltration of

TABLE 4
SUMMARY OF POSTOPERATIVE COMPLICATIONS IN 180 CASES

Complication	Cases
Wound infection	3
Wound dehiscence	2
Prolonged fever	3
Postoperative peritonitis	1
Postoperative atelectasis	1
Vascular pulmonary embolism	1
Acute femoral thrombophlebitis	2
Delayed bronchobiliary fistula	1
Acute urinary retention	1
Adhesions	1
Postoperative hemorrhage (from the uterus)	1
Peritonitis	2

polymorphonuclear cells was extensive now and subintimal edema of the arteries was more frequently seen.

Eleventh Day—Edema was almost entirely absent now and there was moderate fibrosis. Polymorphonuclear cells were in great profusion now and micro-abscesses were common. Venous thrombi were common. Bile and blood pigment were commonly found while sub-

1

was frequently replaced by massive fibrosis. Subperitoneal hemorrhage persisted and subintimal arterial edema was common.

Thirtieth Day—Extensive fibrosis was still evident indicating a fairly complete state of repair. Cellular infiltration was almost entirely

absent although plasma cells and giant cells were frequently seen. Collagen was commonly hyalinized. Moderate hemorrhage was still present in all parts of the wall while blood pigment and subcutaneous edema were commonly seen. Micro-abscesses were occasionally seen.

TREATMENT AND RESULTS

Cholecystectomy was the operation carried out in the 100 cases studied completely although in the original number of 137 cases, cholecystostomy was done in 12 cases.

Three of the 100 patients died. 2 deaths were from peritonitis, while 1 was from uncontrollable postoperative hemorrhage from the incision. Most patients who underwent cholecystectomy had no further symptoms.

In many of the cases cholecystectomy was technically very difficult because of the severe inflammatory reaction, edema and distortion present. It seemed that earlier operation would obviate many of the technical hazards.

From Table 2 it can be seen that most patients recovered satisfactorily in view of the severe pathologic changes present.

SUMMARY

One hundred cases of gangrenous cholecystitis were studied in detail clinically and pathologically. These cases represented about 2.5 per cent of all cases of cholecystic disease in which operation was performed while they were about 33 per cent of all cases of acute cholecystitis in which surgical exploration was performed at the Clinic. Males and females were affected about equally while 57 per cent of the patients were more than 50 years of age. Symptoms were severe when patients were seen early in delayed cases the symptoms were often minimal.

A palpable gallbladder was present in 30 per cent of cases. Obstruction of the cystic duct was present in 93 per cent of cases, while in 80 per cent this obstruction was due to a gallstone impacted in the duct. Perforation of the gallbladder was present in 84 per cent of the cases there were no free perforations in this series.

Histologically there were massive necrosis congestion edema

Cholecystectomy although difficult in many of these 100 cases with 3 deaths.

CONCLUSIONS

- 1 Most cases of gangrenous cholecystitis are primarily obstructive in nature owing to a stone in the cystic duct
- 2 Infection is commonly present, but seems to play a secondary role
- 3 Circulatory lesions are predominant and perforation is frequent
- 4 Generalized peritonitis is rare presumably because of the walling off influence of surrounding structures
- 5 The treatment of choice in gangrenous cholecystitis is early operation the operation of choice is cholecystectomy although in selected cases cholecystostomy is advisable
- 6 Results of cholecystectomy in cases of gangrenous cholecystitis are generally good
- 7 The best treatment for gangrenous cholecystitis lies in prophylaxis cholecystectomy early in the course of the disease as 88 per cent of this series had had previous attacks

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ACUTE PSEUDOMEMBRANOUS ENTERITIS OR ENTEROCOLITIS: A COMPLICATION FOLLOWING INTESTINAL SURGERY

CLAUDE F. DIXON AND RODGER E. WEIDMANN

Acute pseudomembranous inflammation involving the mucosa and submucosa of the gastro-intestinal tract has been studied by pathologists in connection with severe infectious diseases, serious poisoning and severe constitutional disorders. Except in the acute severe diarrheal maladies or in dysentery the clinical manifestations of the condition have not been thoroughly understood. Pathologists, also often have been unable to ascribe clinical importance to pseudomembranous lesions of the digestive tract found at necropsy.

Such lesions apparently follow surgical procedures sufficiently often to be of importance. Finney in 1893 described a patient on whom he had successfully performed gastro-enterostomy but who died of severe "diphtheritic" colitis on the fifteenth postoperative day. Pender and Bernheim, in review of cases encountered at Mount Sinai Hospital in New York, called attention to the pathologic aspects of the lesions and suggested important factors in etiology and pathogenesis. Surgeons have become increasingly aware of this disorder in the study of postoperative mortality. There is, however, insufficient information available regarding incidence, etiology, pathogenesis, clinical manifestations and treatment. This lack of information has prompted us to carry out this study.

At the Mayo Clinic, acute pseudomembranous ileocolitis has been encountered at necropsy in cases in which a wide variety of both medical and surgical conditions have existed.¹ In many cases these inflammatory intestinal lesions were an important, or the sole cause of death. The lesions have been observed at postmortem examination in cases in which death had followed operations on brain, spinal column, breast, gallbladder, uterus, stomach or other organs. They also have occurred from a variety of causes in nonsurgical cases; these will be given further study.

Our interest was stimulated by the recovery, under treatment, of 2 patients who, following radical resection of the colon, presumably had mild or moderate acute postoperative pseudomembranous ileocolitis. These cases are included in our series of 23. Twenty more cases of the 23 were secured when we reviewed Clinic records of a period of seven and a half years. Our survey included records of all cases in which the

patients died following operation on the small or large intestine or the rectum and in which the pathologists discovered significant pseudomembranous lesions of the mucous membrane of the stomach or of the small or large intestine. Finally in 1 case of the 23 permission for necropsy was not obtained but the clinical manifestations strongly suggest that the patient died of acute pseudomembranous enterocolitis. Several of the cases, including the 2 nonfatal ones mentioned, were observed by one or both of us.

INCIDENCE

Frequency with which the lesions occur cannot be determined in this study but, it appears that pseudomembranous lesions were more frequently encountered in the last eighteen months than earlier in the period of study. The reason is not apparent and the increase occurred in spite of use of sulfonamides in preoperative preparation for intestinal surgery. The 23 cases of pseudomembranous enteritis encountered at the Clinic during the period from January, 1940 to June, 1947 inclusive occurred as follows: 1 in 1940, 3 in 1941, 1 in 1942, 3 in 1943, 1 in 1944, 1 in 1945, 6 in 1946, 7 between January 1, 1947 and June 30, 1947 inclusive. The incidence was not increased in any particular season or month; only 5 cases occurred in the months of June through September in the 7½ year period.

pected, however, because of the greater number of older persons who require major intestinal surgery.

ETIOLOGIC FACTORS

Anatomic Distribution.—The lesions often involved the duodenum only, jejunum only, or most of the small bowel, terminating sharply at the ileocecal junction. Intrinsic factors of mechanical or circulatory nature seem to be important. In more typical varieties of our series lesions were present largely in the ileum and superior portion of the colon (Table 1).

Circulatory Disturbances.—Acute, subacute and chronic infarctions usually result in degeneration and necrosis of the entire bowel wall, the extent depending on the degree of ischemia. Congestion of the intestine as a result of congestive heart failure, chronic pulmonary disease or portal hypertension was noted by Boeckx as an important predisposing factor of many inflammatory changes.

Premer and Berthoin were impressed with the importance of vascular phenomena of the mucosa and submucosa of the intestine in production of extensive pseudomembranous change. They pointed out that shock is distinguished by the presence of dilated usually blood-filled venules and capillaries, early relative acellular submucosal and mucosal edema, pericapillary hemorrhages and finally focal mucosal necrosis which by fusion, extension and secondary infection give rise to the more extensive pseudomembranous lesion. They reviewed the development of local tissue changes in the presence of shock and postulated that focal necrosis progressing to confluent denudations, may be the result of widespread circulatory disturbances of severe shock.

Moon has shown that atony of the bowel is encountered in animals in which shock is induced experimentally. The mucosa becomes congested, edematous and takes on a purplish velvety appearance.

TABLE I

LOCATION OF PSEUDOMEMBRANOUS LESIONS IN CASES IN WHICH SHOCK FOLLOWED 1 TO 4 DAYS AFTER SURGERY

Portion of Gastro-intestinal Tract	Patients
Esophagus	4
Stomach	5
Duodenum	3
Ileum	7
Cecum	10
Colon	8

Total equals 45 only because lesions were often multiple given as

Bloody mucous diarrhea and vomiting of bloody fluid often precede death in induced severe shock.

Toxic Infections and Systemic Disorders.—Bockus stated that severe "membranous" enteritis is associated with pyemia, uremia, diphtheria and poisoning from arsenic and mercury. Extensive destruction and sloughing of the intestinal mucosa are encountered in terminal stages of many serious constitutional disorders that:

result by inflammation of the intestine.

Mention should be made of lesions of the intestine associated with the terminal stages of uremia. Extensive necrotic lesions of the colon and occasionally of the stomach, may hasten death in these patients.

and the pathogenesis is not clearly understood. Strecker induced extensive inflammatory intestinal lesions experimentally by the simple process of intravenous injection of 200 cc. of 10 and 20 per cent urea.

We cannot identify the exact role of peritonitis or postoperative obstruction in the development of pseudomembranous lesions. Why these pseudomembranous inflammations have not been reported more frequently in association with these more commonly encountered complications is not understood. The toxic factor of the extensive infection and severe debility of the patient must be of great importance in the predisposition of the intestine to development of serious intrinsic alterations.

The role of infection in development of pseudomembranous lesions is difficult to evaluate. It is doubtful that bacterial irritants are primary factors except in rare instances when virulent organisms of the bacillary dysentery group from an unusual source are involved. In most cases with which this report is concerned patients had been hospitalized preoperatively and had been given specific chemotherapeutic agents to prepare the bowel for surgery. Cultures of fecal discharges in a few cases were negative for the usual bacillary or parasitic agents which produce primary enteritis.

Secondary infection of the denudations, produced primarily by unidentified causes, would be a natural sequel. Resident organisms of the bowel can produce serious local inflammatory changes as well as severe toxic systemic disturbances. Importance of this infection is suggested by the marked purulent character of the fecal and intestinal discharges, the rise of body temperature and the presence of an acute inflammatory process in the mucosa of the involved intestine. However, these are relatively late developments in the clinical picture.

PATHOLOGIC FACTORS

The pseudomembranous (membranous, croupous, diphtheritic, fibrinous) form of enteritis is characterized grossly by the presence of a yellowish gray or grayish brown or green distinct membrane more or less loosely adherent to the underlying superficially eroded mucosa. In early stages there is minimal erosion and the membrane is easily brushed away but the increasing loss of mucosa is attended by firmer adherence of membranous exudate. The involved segment of bowel is somewhat dilated, congested on its serosal surface and apparently partially atonic. Perforation as a result of the enteritis is rare unless necrosis of the entire wall in turn as a result of infarction

is present. In one case there was an infarct in the jejunum and the pseudomembranous lesions involved both the infarcted and unin-farcted portions of intestine. The lesions in these cases appear to extend by confluence of myriads of focal erosions or ulcerations. Early lesions may however be adjacent to lesions in more advanced stages. Acute inflammatory change of the muscular and serosal layers usually does not appear and often there is surprisingly little edema and congestion. However we identified acute early inflammatory changes in several of our cases.

Histologically the most marked alteration is in the submucosal layer where there are intense hyperemia and vascular engorgement. In later stages there is rather marked edema of the stroma of the mucosa and submucosa with extensive intercellular exudation of erythrocytes polymorphonuclear leukocytes and many macrophages and lymphocytes. Occasionally giant cells and focal necrosis are present. The mucosa is not entirely absent and the partially denuded surface is covered by a dense collection of fibrin leukocytes, lymphocytes, erythrocytes and innumerable bacteria. Not infrequently edema and cellular infiltrations of the muscular and serosal coats are seen.

Penner and Bernheim were impressed with the dissimilarity of these histologic changes to any of the usual inflammatory lesions of the intestine. The erythrocytic exudation was thought to be due more to diapedesis than to actual capillary disintegration and vascular changes were striking.

Necropsy revealed frank generalized or localized peritonitis in 12 cases. In 1 of the 12 cases an unsuspected obstructing carcinoma was found superior to the site of a recently resected obstructing carcinoma. In 1 additional case there was obstruction of that portion of the intestine which formed a

CLINICAL MANIFESTATIONS

A review of the records of 20 cases in which pseudomembranous intestinal lesions were found at necropsy and of 3 additional cases, 2 nonfatal, in which acute pseudomembranous enterocolitis was thought to have been present during the postoperative period reveals several clinical manifestations that may have suggested the presence of enteric lesions (Table 2).

The most striking picture is that of a rapidly progressing circulatory

and the pathogenesis is not clearly understood. Strecher induced extensive inflammatory intestinal lesions experimentally by the simple process of intravenous injection of 200 cc. of 10 and 20 per cent urea.

We cannot identify the exact role of peritonitis or postoperative obstruction in the development of pseudomembranous lesions. Why these pseudomembranous inflammations have not been reported more frequently in association with these more commonly encountered complications is not understood. The toxic factor of the extensive infection and severe debility of the patient must be of great importance in the predisposition of the intestine to development of serious intrinsic alterations.

The role of infection in development of pseudomembranous lesions is difficult to evaluate. It is doubtful that bacterial irritants are primary factors except in rare instances when virulent organisms of the bacillary dysentery group from an unusual source are involved. In most cases with which this report is concerned patients had been hospitalized preoperatively and had been given specific chemotherapeutic agents to prepare the bowel for surgery. Cultures of fecal discharges in a few cases were negative for the usual bacillary or parasitic agents which produce primary enteritis.

Secondary infection of the denudations, produced primarily by unidentified causes, would be a natural sequel. Resident organisms of the bowel can produce serious local inflammatory changes as well as severe toxic systemic disturbances. Importance of this infection is suggested by the marked purulent character of the fecal and intestinal discharges, the rise of body temperature and the presence of an acute inflammatory process in the mucosa of the involved intestine. However, these are relatively late developments in the clinical picture.

PATHOLOGIC FACTORS

The pseudomembranous (membranous, erosive, diphtheric, fibrinous) form of enteritis is characterized grossly by the presence of a yellowish gray or grayish brown or green distinct membrane more or less loosely adherent to the underlying superficially eroded mucosa. In early stages there is minimal erosion and the membrane is easily brushed away but the increasing loss of mucosa is attended by firmer adherence of membranous exudate. The involved segment of bowel is somewhat dilated, congested on its serosal surface and apparently partially atonic. Perforation as a result of the enteritis is rare unless necrosis of the entire wall, in turn as a result of infarction

Circulatory collapse which was almost invariable in our series, was associated with the clinical onset of intestinal complication. The interval between the state of severe shock and death was so brief in many cases that it seemed unlikely that extensive pseudomembranous lesions could have developed as a result of or subsequent to the state of circulatory deficiency.

Signs and symptoms of intestinal dysfunction were present in most cases but were particularly diagnostic in those in which peritonitis or other lesions were not found. Abdominal pain diffuse and often cramping in nature occurred in thirteen cases and usually preceded onset of collapse by only a few hours. Significant abdominal tenderness was present only when there was peritoneal irritation from other causes.

Mild to moderate distention was noted in all but 4 cases and in several a preliminary roentgenogram of the abdomen revealed an increased amount of gas throughout the intestinal tract. Distention was principally of a paralytic type and borborygmi almost always absent. Dilatation of the bowel increased fairly rapidly after onset of other clinical manifestations, in spite of decompression by continuous suction.

Diarrhea or frequent fecal discharges from artificial stomas were present in only 9 of the 23 cases. Since some of the patients had undergone either ileostomy or colostomy increased fecal output, when present, caused considerable loss of fluid, electrolytes and nutritional substances. In 1 case in which the patient survived, discharge of bright green, thin, fecal material from a transverse colonic stoma strongly suggested the possibility of a jejunocecal or duodenocolic fistula. In other cases fecal discharge from the colonic stoma was described as "rice-water stool" similar to that of infectious diarrhea. The fecal discharge of the 3 surviving patients became increasingly foul and purulent, and it contained nondescript shreds or plaques of material thought to be fibrin or sloughed tissue. Most of the patients gave no signs of increased intestinal activity or marked loss of fluid. Bleeding from the bowel was not recorded. In cases in which there was no significant diarrhea it is probable that the loss of extracellular and intracellular fluids into the lumen of the intestine was considerable and would account for the circulatory collapse.

Nausea or vomiting was present to some degree in all cases but, in most, use of an indwelling gastric tube gave relief. When the upper part of the gastro-intestinal tract was involved the vomitus or aspirated material was thick and often dark red or brown strongly

collapse extremely resistant to supportive and resuscitative measures, resulting in irreversible shock and death in a matter of hours. The similarity in this respect to Asiatic cholera has been noted by several surgeons and clinicians and the clinical signs to which the acute intestinal lesions give rise may rest on a physiologic basis similar to those of Asiatic cholera.

In the cases in which associated serious pathologic changes were found such as peritonitis, obstruction, intestinal perforation or infarction, there appeared to be little evidence on which a surgeon could depend to diagnose the intestinal lesions. Patients were extremely ill and primary symptoms and signs were those usually associated with serious intra-abdominal complications. However, the onset of acute circulatory collapse with profound shock was significant. This severe collapse, as has been said, usually is irreversible and death soon

TABLE 2

SYMPTOMS AND SIGNS ASSOCIATED WITH CLINICAL COURSE OF POST-OPERATIVE
INTESTITIS IN 23 CASES

Symptom or Sign	Patients
Abdominal pain	13
Circulatory collapse	24
Diarrhea or frequent stool discharges	9
Dysentery	10
Vomiting	11
General fever	11

Total exceeds twenty three because multiple symptoms often occurred in given case.

follows. In 2 cases a state of collapse was noted only at a terminal

by extreme emaciation, pallor and weakness. In spite of blood transfusions, convalescence was very slow and the time required to regain strength and weight was unusually prolonged.

In our series, shock during the early postoperative period was

Thus, we cannot confirm clinically their hypothesis that the motor disturbances incident to postoperative or traumatic circulatory deficiencies were major factors in the pathogenesis of these lesions.

ment this is particularly important if as is likely the state of shock is resistant to antishock measures. The abdomen is usually mildly to moderately distended tenderness is diffuse nonlocalizing and mild. Vomiting may be present. Although of little value from the standpoint of early diagnosis, later in the course the fecal contents become extremely foul, serous or seropurulent and may contain identifiable portions of pseudomembrane.

Differential diagnosis of this condition from other commoner postoperative complications in the abdomen is extremely difficult. The onset of peritonitis is similar to that of simple or strangulating intestinal obstructions and differentiation may never be possible. In several of our cases, the clinician's impression was that pulmonary embolism or coronary occlusion caused death. Laboratory determinations help only in ruling out the possibility of cardiac or pulmonary complications. Enterocolitis may occur at any time in the postoperative period but, in our series, it was seen most often between the fourth and fourteenth postoperative days, when commoner serious complications also occur. Differential diagnosis may be deferred until vigorous supportive treatment for circulatory collapse is well under way. By this time if the underlying condition were strangulating obstruction, mesenteric thrombosis, peritonitis or the like signs would be likely to be unequivocal. It must be pointed out, however that pseudomembranous inflammation may occur in association with the conditions just named. Also if resection or other operative procedures on the intestine are carried out for these or other conditions, the possibility of mucosal and submucosal lesions should be kept in mind.

TREATMENT

In consideration of prevention of the lesions, it would be desirable to determine the important etiologic factors. Early and adequate management of postoperative shock possibly would help prevent certain vascular disturbances of the intestinal mucosa and submucosa, which may be the basis for this complication. Adequate preoperative preparation, directed at correcting malnutrition, marfan anemia, avitaminosis and protein deficiency should increase resistance of the intestinal mucosa to toxic factors. Control of renal function during the postoperative period would reduce danger of secondary intestinal inflammation, as a result of azotemia. Preoperative use of various sulfonamides does not seem to be important in prophylaxis. In our series, before operation the majority of patients received sulfonamides as well as saline cathartics and colonic irrigations. The effect of too vigorous preparation or the local toxic effect of chemotherapeutic

suggestive of extensive extravasation of blood into the lumen of the tract. In 1 case in which extensive infarction of the jejunum had occurred and pseudomembranous lesions involved both infarcted and noninfarcted portions blood was frankly present in the aspirated material. In several instances the quantity of material aspirated was excessive.

Fever was a relatively late sign. In most of the cases the postoperative temperature preceding clinical onset of acute enteritis, was not remarkably elevated and in most of the uncomplicated situations, it had been normal just prior to manifestations of intestinal lesions. With collapse the temperature was usually subnormal from twelve to twenty-four hours preceding death or until the patient responded to supportive measures. The body temperature of patients who survived longer than twenty-four hours rapidly rose to 103° or 104° F. and patients appeared exceedingly toxic. This was thought to have indicated the presence of unrecognized intestinal lesions. Of the 3 patients who recovered 1 remained in the febrile state thirty-six hours and the other six days. It is believed, as Penber and Bernheim pointed out, that terminal or late elevation of temperature represented secondary invasion by pathogenic micro-organisms as well as systemic effects of toxicity arising from lesions infected by these organisms.

DIAGNOSIS

In the past, we did not suspect the presence of significant, acute postoperative pseudomembranous enteritis. The condition was found at necropsy. However increased incidence during the past year has resulted in increased awareness of this complication and the surgeon in charge suggested severe enterocolitis in 4 of our cases in 2 of which the patients survived. Even yet, nevertheless, it seems that positive diagnosis of acute pseudomembranous enterocolitis can be established only at necropsy² or by identification of a membranous cast in the fecal discharges.⁴ Such casts are seen relatively late in the course of the disease often when healing is well under way.

Successful management demands that the condition be recognized at once. From our experience certain manifestations strongly suggest the presence of pseudomembranous enterocolitis. They have been discussed earlier in this paper as clinical manifestations. We believe, however, that there is some point in summarizing them here. Acute cramping, diffuse abdominal pain with or without diarrhea, or frequent or constant discharge from a colonic stoma may be the earliest signs. In many cases, however severe circulatory collapse usually unexplained, may precede the onset of extensive intestinal involve-

Antibiotics, preferably penicillin in doses up to 100,000 Oxford units every three hours, should be instituted to assist the intestinal wall in combating secondary invasion by certain pathogenic micro-organisms, which appears inevitable when sufficient damage to the mucosa and submucosa has taken place. Streptomycin has not, so far as we know, been used with success in the treatment of this condition. Nevertheless, since evidence exists of the effectiveness of this antibiotic preparation against the pathogens normally resident in the lower part of the intestine streptomycin may be indicated in combating secondary invasion.

If fecal discharges are excessive some good effect may be obtained from codeine, pantopon, dilaudid or morphine in combating peristalsis. We suggest that these drugs be used sparingly because of the precarious circulatory state and also because a certain amount of catharsis may be desirable if toxic materials of etiologic significance are to be eliminated from the intestine. If possible campborated tincture of opium may be judiciously used.

The question of the value of poorly absorbed or nonabsorbable sulfonamides, given either orally or by gastro-intestinal tube cannot be answered from this study. On first consideration it would appear advisable to combat secondary intestinal invasion of resident organisms by adequate doses of sulfonamides but this has not appeared to be of much value. In addition the question of irritation or toxicity consequent on preoperative use of sulfonamides remains to be settled.

Laparotomy in the presence of acute pseudomembranous enteritis, is contraindicated unless other intra-abdominal lesions necessitate such surgical treatment. In some instances the presence of a severe process such as perforation of a viscus, leakage at an anastomosis or strangulating obstruction may be so strongly suggested that no other course is open. Operation on the bowel itself may be hazardous when the pseudomembranous lesions of the mucosa are of any great extent.

REPORT OF CASES

From the 40 cases in which necropsy revealed the presence of severe gastric or intestinal pseudomembranous lesions of the mucosa, reports of 4 are given in some detail. These cases are considered typical of those in which the pathologist considered the pseudomembranous inflammatory lesions to be one of the most important contributing causes of death. The entire series of 33 cases is summarized in Table 5.

agents on the intestinal mucosa cannot be determined but it is believed that neither was of significance in production of the lesions in our cases.

In spite of the fatal outcome in most cases of our series, in which extensive pseudomembranous enterocolitis existed either alone or in combination with serious intra-abdominal disturbances, we believe that the prognosis is not uniformly hopeless. Heretoe effects are needed, though if many of the patients are to survive. The 3 patients in our series who presumably had a form of this complication following surgery on the colon and who had survived give us hope and have formed the basis for our suggestions of treatment.

Definitive treatment of pseudomembranous enterocolitis must be largely on empiric grounds until basic etiologic and pathogenic factors are understood. Of primary importance are realization of the possibility of presence of the entity, prompt recognition of related symptoms and, during the ensuing hours of antishock treatment, an attempt to make a tentative or a working diagnosis.

Aggressive and prompt replacement of fluids, preferably in the form of whole blood and plasma, must follow recognition of the down hill course. If cardiac and pulmonary complication can be reasonably discounted, we advocate intravenous injection of 1,000 to 2,000 cc. of whole blood and additional plasma up to 2,000 to 3,000 cc. depending on the response of the circulatory system. Saline solution and solution of dextrose can be given at the same time as the blood and plasma or in the intervals between their administration. In severe collapse, direct exposure of the veins for venipuncture may be resorted to and even multiple venotomies can be instituted. It is preferable not to exceed 0 to 15.5 gm. of sodium chloride in the first twenty-four hour period or in any period, until the average concentration of blood chlorides can be accurately determined. With renal function depressed as a result of hypotension and the circulatory state, dextrose in water can be judiciously given in adequate quantities but not to excess. Depending on loss of fluid and electrolytes by fecal discharge or upper gastro-intestinal aspiration, the quantity of saline solution or of solution of dextrose will vary but 4,000 cc. of water containing dextrose or of saline solution per twenty-four hours would be considered ample.

In the presence of marked circulatory collapse or rapidly developing tissue ischemia, administration of oxygen by inhalation would be an important adjunct to the foregoing supportive treatment.

TABLE 2—Continued

		Cases
Postoperative day on which death occurred†	Eighth day or sooner	11
	Between the forty-third day inclusive	3
	Not recorded	5
Symptoms	Shock	21
	Distention	19
	Abdominal pain	13
	Diarrhea	8
Part found involved (at necropsy)	Ileum and colon	4
	Ileum only	3
	Duodenum only	2
	Ileum and ileum	2
	Esophagus, stomach and ileum	1
	Esophagus, ileum and colon	1
	Stomach and duodenum	1
	Ileum, ileum and colon	1
	Duodenum and jejunum	1
	Ileum only	1
	Descending colon only	1
	Sigmoid only	1
	Low or sigmoid and rectum	1
Associated condition found at necropsy‡	Peritonitis only	1
	Obstruction	2
	Carcinoma of bowel	2
	Perforated duodenal stump plus jejunal gangrene	1
	Peritonitis and bronchopneumonia	1
	Vesical abscess	1
	Acute sinusitis	1
	Perforation of ileum	1
	Colonic dilatation	1
	Pelvic abscess	1
	Sigmoid carcinoma and nonfatal pulmonary embolism	1
	H ₂ thrombosis and pyelonephritis	1
	Nonfatal pulmonary infarction only	1
	Rectal carcinoma only	1

† Twenty-one of the patients died; 2 lived.

‡ Total number of deaths as twenty-one; 2 patients lived. One case is not included here because necropsy data were not obtained.

TABLE 3
SUMMARY OF 23 CASES

		Cases
Age	78 years to 1 day	23
Sex	Males 13 females 10	23
Preoperative diagnosis	Carcinoma lower bowel only	12
	Chronic ulcerative colitis with fistulae	9
	Perforating diverticulitis with pericolic abscess	1
	Carcinoma of lower bowel and chronic ulcerative colitis	1
	Congenital stricture of jejunum	1
	Stricture of abdominal aorta	1
	Perforating appendicitis	1
	Indeterminate chronic recurring intestinal obstruction	1
	Carcinoma of bladder with pericervical fistula	1
	Gastroperforate fistula with postperitoneal abscess	1
Operation	Regional enteritis with enterovesical fistula	1
	Intestinal resection only	6
	Enterostomy only	3
	Intestinal resection, anastomosis and colectomy	3
	Intestinal resection with anastomosis	1
	Appendectomy with drainage	1
	Intestinal anastomosis only	1
	First stage of colectomy and double-barrelled ileostomy	1
	Plastic operation on aorta	1
	First stage of abdominoperitoneal resection	1
	Exploration and pyeloplasty	1
	Exploration and freeing of adhesions	1
	Ureteropyelostomy	1
	Disconnection of gastro-enterostomy, gastric resection, resection of part of jejunum, closure of colon	1
	Resection of right portion of colon and of aorta, partial cystectomy	1
Postoperative day of probable onset of enterocolitis	Ninth day or less	16
	Fourteenth to thirty-eighth day inclusive	6
	Not recorded	1

involved the entire circumference of the bowel was found at that point. In the sigmoid the annular obstructing carcinoma previously described was encountered. Perforation had not occurred.

Histologically the lesions of the esophagus, stomach and small intestine consisted of diffuse superficial ulceration and acute inflammatory changes of the mucosa and submucosa, with a layer of fibrinopurulent exudate over the surface.

CASE 2—A white man, 60 years of age, was first seen at the Clinic February 27, 1946. He complained of having had diarrhea without bleeding periodically for many years. Frank symptoms of obstruction were lacking. There had been increasing loss of weight with loss of 8 pounds (3.6 kg.) in the past month. For a short time prior to admission, the man also had had dysuria and polyuria of increasing severity. After examination, a diagnosis of perforating diverticulitis, with peritonigastral abscess, was made. In addition, benign prostatic hypertrophy was present. On March 16, 1946, after adequate preparation, the abdomen was explored and it was found that the lesions were confined to the pelvis, where a relatively hard, fixed mass was discovered above and behind the bladder. Metastatic lesions were not noted. Loop colectomy utilizing the transverse colon, was carried out with the view of resecting the mass and the corresponding portion of the sigmoid in six to nine months. Until approximately twenty hours after operation, the patient appeared to be in good condition. At that time he complained of severe upper abdominal pain and, shortly thereafter, sudden and profound circulatory collapse occurred. The possibility of a cardiac accident was seriously considered. He was given 500 cc. of blood and 500 cc. of plasma, but maintained a rapid downward course and died thirty hours postoperatively. There was no record of any vomiting or of fecal discharges from the colon, stomach or rectum. The clinical impression was that postoperative shock had occurred.

Postmortem Findings—The peritoneal cavity did not contain free fluid but the surfaces seemed somewhat dull, dry and granular. There were early fibrous adhesions between intestinal loops. Cardiac or pulmonary lesions of note were not found. The entire esophagus was ulcerated and gangrenous and the wall was congested. Mediastinitis was absent. The entire intestine was markedly distended and dark red. In the colon and extending into the inferior portion of the ileum, the mucous membrane was markedly congested, early necrosis and pseudomembrane were present. The sigmoid was tortuous and adherent to the dome and posterior wall of the bladder. The large pelvic mass was composed of dense, fibrous tissue and surrounded the sigmoid, almost completely obstructing the bowel at the rectosigmoid junction. An abscess, 1 cm. in diameter was in the dome of the bladder.

On histologic examination, the esophageal epithelium was seen to have entirely sloughed and there were early necrosis and marked congestion of the mucosa of the ileum and colon. The lesion of the sigmoid was the site of inflammation.

CASE 1—A married woman, 67 years of age, was first seen at the Clinic on April 7, 1941. She gave a history of attacks of nausea and vomiting of one year's duration, loss of weight and recurrent lower abdominal pain of two-month duration and recent intermittent diarrhea and constipation without melena. A diagnosis was made of multiple carcinomas of the colon, one in the mid-ascending and one in the cecum. She also had cerebral arteriosclerosis with mild residual manifestations of hemiplegia which had occurred four years previously. After preoperative administration of sulfaguanidine, in the hospital, exploration was performed on April 12, 1941. An obstructing lesion in the sigmoid was far advanced and required early attention. Accordingly loop colostomy of the transverse colon was carried out with the idea of performing anterior segmental resection at a later stage. Resection of the right portion of the colon also was planned for a subsequent stage. Immediate convalescence was satisfactory and the patient was discharged from the hospital on the twenty-fourth postoperative day. She was readmitted to the hospital on the thirty-ninth postoperative day complaining of severe abdominal distress, distention, nausea and vomiting. The presence of diarrhea was not recorded. She gave a history of having eaten a salad which "didn't agree with her." At this second admission she was thought to have an obstruction of the small intestine. Gastro-intestinal suction was started. The following day copious amounts of thick, black liquid were obtained by aspiration from the upper part of the gastro-intestinal tract. Roentgenograms of the abdomen did not reveal evidence of distention. Within twenty-four hours after admission increasing circulatory collapse developed and profound shock supervened on the fortieth postoperative day. In spite of transfusion of 1,500 cc. of whole blood, and intravenous injection of 800 cc. of solution of sodium, as well as of adequate quantities of dextrose and saline solutions the state of circulatory collapse continued and the patient died on the forty-third postoperative day, May 24, 1941. The clinical impression of the causes of death was given as follows: (1) mesenteric thrombosis, (2) hemorrhagic peptic ulcer, (3) perforation of one of the colonic carcinomas, and (4) strangulated intestine.

Postmortem Findings—The peritoneal cavity contained no free fluid and was free of significant adhesions. The lower part of the jejunum and the upper portion of the ileum were moderately dilated and the serosal surfaces were congested.

The mucous membrane of the esophagus was covered by greenish exudate with underlying superficial ulceration. Similar changes were present at the cardia, along the lesser curvature of the stomach and in the pyloric region.

... areas on
the mucosal
membranes which

given in the last twenty hours. Clinically he was thought to have died of rapidly fulminating, generalized peritonitis.

Postmortem Findings—The peritoneal cavity did not contain free fluid and significant adhesions or gross evidences of peritonitis were absent. The ileum, cecum and remaining part of the colon were moderately dilated. Except in these portions of the gastro-intestinal tract there were no significant intra-abdominal findings. There was a nonfatal right pulmonary embolus, with



Fig. 279.—Wall of the ileum in case 8. The membrane that was stripped from the surface is represented in Figure 280. The following are noteworthy: marked vascular engorgement of the submucosa, much destruction of the mucosa and extensive edema of all coats (hematecylin and eosin $\times 45$).

early infarction and collapse of both lower lobes. The mucous membrane of the entire ileum and colon was covered with a brittle greenish pseudomembrane (Fig. 278) which was friable and could be stripped away easily. Beneath, the surface was congested and inflamed. Portions of mucous membrane remained in the ileum after the pseudomembrane had been stripped off (Figs. 279 and 280) but, in the colon, mucous membrane appeared, on gross inspection, to be entirely absent and the membrane extended into the muscularis

CASE 3—A white man, 43 years of age, was first seen at the Clinic January 7, 1917. His chief complaints were of having had a feeling of fullness in the rectum for three months and recently slight bleeding with defecation. He had not lost weight nor had he had symptoms of obstruction. Carcinoma was present in the lower part of the rectum. After adequate preoperative preparation, including use of sulfonamides, the rectum was resected on January 14, 1917, by the abdominoperitoneal method of Miles. Intra-abdominal metastasis was not noted. On the third postoperative day secondary closure of the peritoneal wound was effected. The course until the fourth postoperative day was uneventful. On the night of the fourth postoperative day the patient



Fig. 378—Mucosal surface of the ileum in case 3. A portion of the membrane has been stripped away and is lying partially free and folded on itself.

began to perspire, became nauseated and vomited two or three times. After this, severe, copious watery discharges issued from the colonic stoma. The next morning the man was in a state of shock. His pulse rate was 160, blood pressure was 70 mm. of mercury systolic and 0 diastolic. He was given 500 cc. of whole blood and 500 cc. of plasma and considerable symptomatic improve-

ment ensued and another 500 cc. of whole blood. His temperature rose to 105° F. His condition became rapidly worse and he died thirty hours after the onset of symptoms in spite of massive doses of penicillin and streptomycin.

sixth postoperative day he was up and about and was feeling well. On his thirty-second postoperative day, however, he complained of severe cramping abdominal pains which came on suddenly and which were followed by vomiting and frequent discharges from the ileal stoma. Temperature had been normal for several days preceding the episode. Severe circulatory collapse with increasingly rapid and feeble pulse developed, and temperature rose sharply to 105° F. The man died on the thirty-third postoperative day. The clinical impression was that acute exacerbation of chronic ulcerative colitis, with ileal progression or perforation of an acute ulcerated lesion had taken place.

Postmortem Findings.—The peritoneal cavity contained 500 cc. of clear straw-colored fluid (ascites?) but there was no evidence of peritonitis. The mucosa of the lower part of the jejunum was covered by a thin, yellowish pseudomembrane (Fig. 281) which, when peeled away, pulled some of the un-

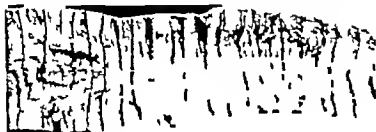


Fig. 281.—Mucosal surface of the lower part of the jejunum in case 4. The thin membrane is partially detached in several places and wrinkled in others.

derlying mucosa with it. The lesion became more pronounced as examination progressed toward the ileum, and the ileum was involved as far as the stoma. Subacute and chronic inflammatory disease was present in the mucosa and submucosa of the colon but acute perforation or active, progressing ulceration were not seen.

Histologically the mucosal epithelium of the lower part of the jejunum and the upper part of the ileum was partially destroyed. There was evidence of considerable exudative reaction and fibrosis of the mucosa (Figs. 282 and 283) and many tubercles were found.

chiefly lympho-
cytic in nature.

Histologically in the ileum were some edema and lymphocytic infiltration of the mucosa and submucosa. About half of the mucous membrane had sloughed away (Fig. 290). In the colon, only a small piece of mucosa remained and this was edematous, congested, and infiltrated by lymphocytes and few polymorphonuclear leukocytes. Also, distended blood vessels (evidence of congestion). The submucosa was markedly edematous.

CASE 4.—A white man, 69 years of age, had been seen and treated repeatedly at the Clinic since 1853 because of chronic ulcerative colitis. On his last admission, March 22, 1947, he gave a history of frequent rectal bleeding

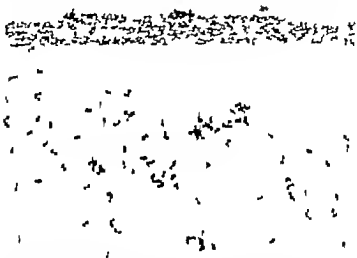


Fig. 290.—Detached membrane in case 3. A dense network of fibrin contains numerous cellular exudates and detached pieces of the mucosal epithelium and glands (leucocytes and some X200).

of four months' duration. An adenocarcinoma of the rectum, grade 2, was discovered and it was decided to perform ileostomy and total colectomy in multiple stages. After preoperative preparation with sulfonamides and colonic irrigations, double barreled ileostomy with separation of the limbs of the loop (first stage) was carried out on April 4, 1947. On April 5, partial dehiscence of the wound and secondary closure were performed. In the early part of the postoperative course, marked peripheral edema developed and was associated at times with pulmonary and cerebral edema. The case never was definitely determined. Treatment consisted of digitalization and infusion of blood and plasma. Gradually the patient's condition improved and, by his twenty

with postoperative day he was up and about and was feeling well. On his thirty-second postoperative day, however, he complained of severe cramping abdominal pains which came on suddenly and which were followed by vomiting and frequent discharges from the ileal stoma. Temperature had been normal for several days preceding the episode. Severe circulatory collapse with increasingly rapid and feeble pulse developed, and temperature rose sharply to 105° F. The man died on the thirty-third postoperative day. The clinical impression was that acute exacerbation of chronic ulcerative colitis, with ileal progression or perforation of an acute ulcerated lesion had taken place.

Postmortem Findings—The peritoneal cavity contained 400 cc. of clear straw-colored fluid (seros?) but there was no evidence of peritonitis. The mucosa of the lower part of the jejunum was covered by a thin, yellowish pseudomembrane (Fig. 231) which, when peeled away, pulled some of the un-



Fig. 231.—Mucosal surface of the lower part of the jejunum in case 4. The thin membrane is partially detached in several places and wrinkled in others.

derlying mucosa with it. The lesion became more pronounced on examination progressed toward the ileum, and the ileum was involved as far as the stoma. Subacute and chronic inflammatory disease was present in the mucosa and submucosa of the colon but acute perforation or active progressing ulceration were not seen.

Histologically the mucosal epithelium of the lower part of the jejunum and the upper part of the ileum was partially destroyed. There was evidence of considerable exudative reaction and fibrosis of the mucosa (Figs. 232 and 233) and many polymorphonuclear leukocytes, erythrocytes and round cells were present.

round cells. The colon throughout was scarred and its submucosa had undergone marked hyperplasia. In the rectum was an adenocarcinoma, grade 2.

which had spread perirectally and had metastasized to the mesenteric lymphatic structures.

The following fatal case was not examined post mortem and the diagnosis cannot be positively established but its clinical similarity to other fatal cases with *pseudomembranous* enterocolitis is so striking and the circumstances so unusual that it is included in this study.

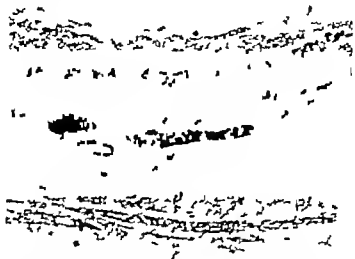


Fig. 282.—Wall of lower part of jejunum in case 6. At the top of the photomicrograph, the membrane, although thin, is rather firmly adherent to the mucosa. Extensive cellular infiltration and edema of the muscular and serosal layers are evident (hematein and eosin, $\times 87$).

CASE 3—A married woman, 66 years of age, underwent abdominal-perineal resection of the distal portion of the colon and rectum in one stage, in 1937 for adenocarcinoma of the rectum, grade 2 (type B, Duke's). Her colon abscesses and recto-vag had been uneventful and she remained in good health. In the year preceding her last visit to the Clinic she had noted recurrent bulging at the site of a single-barreled type of sigmoidal abdominal colostomy and narrowing of the stoma. Crampy pain in the abdomen had occurred frequently preceding the discharge of feces from the colonic stoma. On examination, considerable redundancy of that portion of the bowel which lay in the subcutaneous tissue and over the fascia was found, together with marked narrowing of the stoma. On May 31, 1947, under pentothal anesthesia, a plastic opera-

tion was performed on the stomach and the redundant portion of bowel was amputated at the level of the skin. Only the skin and subcutaneous tissues were incised and two catgut sutures were placed in the anterior fascial layers. The bowel was not otherwise disturbed and the peritoneal cavity was not entered. The woman was dismissed from the hospital on her sixth postoperative day. Until then, feces had not been passed spontaneously by way of the colonic



Fig 283—Higher power view of the mucosal pseudomembranous junction in the pyronin (case 4). Pseudomembrane at the top displays the character of the inflammatory reaction and cell types. A portion of epithelium remains on the right (hematoxylin and eosin $\times 250$).

as several large quantities of liquid feces. On her ninth postoperative day she was readmitted to the hospital, she was vomiting and frequently passing, by way of the stomach, copious, foul-smelling, "rice water" material. Intubation of the upper part of the gastrointestinal tract was begun. Intramuscular

administration of penicillin was started and sulf. isidiazine was given through the gastro-intestinal tube. Early the next day the patient's condition deteriorated rapidly and she went into a state of profound shock. At that time the temperature was 103° F. (axillary), the pulse rate ranged from 120 to 140 per minute and blood pressures were 80 mm. of mercury systolic and 0 diastolic. She was given 1,000 cc. of whole blood and 2,000 cc. partly of solution of dextrose and partly of saline solution. Some improvement was noted but it was not maintained. Later that day 1,000 cc. of plasma and 2,000 cc. partly of solution of dextrose and partly of saline solution were given intravenously. The woman continued to grow sorer and signs of acute arterial occlusion in both lower extremities developed (mild thromboses?). The concentration of blood urea rose rapidly and acidosis increased in the last forty-eight hours of her life. She died on the twelfth postoperative day. Cultures of the discharges from the colonic stoma, made on two occasions, revealed no growth of organisms of the dysentery or typhoid groups. Blood cultures remained negative.

Following are summaries of reports of 8 cases in which the patient survived acute postoperative complications, presumably acute enterocolitis of pseudomembranous type. It is successful treatment in these 8 cases which stimulated our interest in studying this difficult and heterogeneous group of patient.

CASE 6—A white man, 58 years of age first registered at the Clinic August 26, 1946, complaining of rectal distress and urgency of defecation of one year duration. He had noted some nervousness in constipation and some intermittent rectal bleeding. On proctoscopic examination, he was found to have a carcinoma of the rectosigmoid, 14 cm. from the dentate line. After the usual preoperative colonic preparation, resection of the entire pelvic portion of the colon and part of the upper portion of the rectum was carried out, with open anastomosis (end to end) of the descending colon and upper part of the rectum. Colostomy of the transverse loop, complementary type also was done at the completion of the operation. The lesion proved to be an obstructing, perforating adenocarcinoma, grade 2, with peritoneal and nodal involvement by direct extension (type B, Duke). Postoperatively the patient's course was rather stormy. On the third postoperative day nausea, vomiting and mild distention developed. The following day it was necessary to start continuous gastric suction. Mild generalized abdominal tenderness developed, along with moderate distention. On the fifth day the patient's condition was not improved and a large amount of serosanguineous fluid began to issue from the Penrose drain that had been placed in the pelvis. The average temperature was about 100° F. and the pulse rate 120 per minute. Some improvement followed intramuscular injection of penicillin and intravenous administration of sulfadiazine.

On the eighth postoperative day the abdomen became more distended and the man complained of intermittent abdominal pain. In addition, he began frequently to discharge from the colonic stoma, copious amounts of material containing large quantities of serous exudate. The discharged material contained excessive fresh bile later in the day and was practically identical with the material obtained by nasal suction. Because of this, it was thought that the patient might have a jejunocolic fistula. During the night of the eighth postoperative day circulatory collapse rapidly developed and, at 4 a. m. on the ninth postoperative day, he was observed to be in a state of profound shock; his pulse was imperceptible and the blood pressure in the arm could not be read. Immediately 1,000 cc. of whole blood and 500 cc. of plasma were administered and the response was excellent. In the course of the next twenty-four hours, the man received, intravenously, 4,000 cc. of water to which was added dextrose and sodium chloride; also, 2,000 cc. of dextrose and water were given subcutaneously. His temperature rose to 102° F. in the course of this day. In the ensuing day (the tenth postoperative day) his condition slowly improved but he became very pale and appeared greatly emaciated. Discharges from the colonic stoma then became, at first, purulent and foul and after that gradually took on a more normal fecal character. The increased frequency of bowel movement, however, continued until the fifteenth postoperative day. Distention, nausea and vomiting gradually lessened and the patient was able to take nourishment normally by the seventeenth postoperative day. By this time the temperature had returned to normal. The patient's subsequent convalescence was markedly prolonged but otherwise was uneventful.

On June 6, 1947, the transverse colonic stoma was closed intraperitoneally. The patient had some drowsiness, nausea and vomiting, for which gastric suction was required for twenty-four hours on the fifth day after this last operation. He recovered rapidly, however, and was discharged from hospital on the thirteenth day after this last admission. He was without complaint at the time of his discharge from our care two weeks later.

CASE 7—A white farmer, 57 years of age, came to the Clinic on October 14, 1946, complaining of frequency and urgency of defecation for three months. His stools sometimes had been streaked with blood. In addition, he had lost 15 pounds (6.8 kg.). A carcinoma of the rectosigmoid was found. On October 23, 1946, after the usual preoperative preparation of the colon, 60 cm. of bowel, composed partly of sigmoid and partly of the upper portion of the rectum were resected. The descending colon and upper part of the rectum were anastomosed by the open method and at the close of the operation, temporary colostomy was established by the loop transverse method. The lesion was an adenocarcinoma, grade 1 and was classified also as of type B (Dukes). The postoperative course was excellent until the seventh day when in the afternoon frequent, liquid discharges flowed from the colon.

stoma without significant abdominal distress. Within a few hours the patient was in a state of severe shock; he was pale, perspiring and extremely weak. The pulse was extremely rapid and feeble and blood pressure was barely perceptible. He was given 2,000 cc. of a solution which contained dextrose and sodium chloride. 1,000 cc. of plasma also was administered. In addition, large doses of camphorated tincture of opium were administered. Response to these antishock measures was good. Later penicillin was administered intramuscularly.

On the eighth postoperative day 500 cc. of whole blood, as given further to stabilize the cardiovascular system. At that time, the diagnosis of acute enteritis strongly was considered and cultures and smears were made of the fecal discharge from the colonic stoma. These cultures were reported to be negative for organisms of the dysentery and typhoid groups and the smears were free of pathogenic parasites or ova. The patient's condition improved rather promptly thereafter. The temperature, which had risen to 103° F. on the seventh postoperative day, had returned to normal thirty-six hours later. Frequency of the colonic discharges was reduced but the discharged material took on a very foul and purulent character about twenty-four hours after the onset of symptoms. During the ensuing three days, the fecal discharge gradually returned to normal. However, several plaques of firm white substance appeared in the material discharged from the colonic stoma and suggested disintegration of a membranous exudate which had been present in the bowel. More remarkable, however, was the striking change in the patient's appearance from that of health to that of marked emaciation, with pallor and weakness. Furthermore, the profound effects of his illness were demonstrated in the prolonged convalescence, before original weight and strength were regained.

After a prolonged period of convalescence at home the patient returned in good condition and his colonic stoma was closed intraperitoneally on February 12, 1947. His recovery from this procedure was uneventful and he was dismissed from our care about three weeks later.

SUMMARY OF OTHER CASES

Certain data concerning the 16 cases not reported in the foregoing section are worthy of consideration. In 15 of these 16 cases, peritonitis

weak and had intestinal obstruction on admission; the cause of his death, however, was principally peritonitis. Gangrene of some part of the gastro-intestinal tract was present in 5 of the 16 cases and gangrenous gastritis was suspected in another. In the 1 case of the 16 in which there was no peritonitis, the outstanding difficulty probably was renal failure.

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ASEPTIC NECROSIS OF THE HEAD OF THE FEMUR FOLLOWING A MINOR FRACTURE OF THE GREATER TROCHANTER: REPORT OF CASE

ALFRED E. JACKSON AND WILLIAM H. BICKEL

WITH the advent of newer methods of treatment of fractures around the hip the number of cases of nonunion of the femoral neck has been greatly reduced however aseptic necrosis of the head of the femur continues to be a formidable complication.^{1, 2} No cases of aseptic necrosis of the femoral head following fracture of the greater trochanter have been found in the literature.^{3, 4}

REPORT OF CASE

A man 64 years old was brought to the Clinic on November 11, 1943. At that time he stated that three and a half hours previously he had slipped on the sidewalk and had fallen on his knees and then rolled to his left side. He had experienced some pain in the knees and left hip at the time of the accident but was able to arise and walk seven blocks to his place of employment without excessive pain. The pain in the region of the left hip gradually increased and he was brought to the Clinic.

Physical examination disclosed some limitation of motion due to pain in the left hip. Roentgenograms revealed a fracture of the left greater trochanter with minimal displacement of the fragment (Fig. 284).

The patient was admitted to the hospital and placed on a Bradford frame with the left lower extremity elevated. Heat was applied to the upper part of the left thigh and gluteal region. Two weeks after admission to the hospital roentgenograms of the left hip revealed good position of the left greater trochanter. The patient remained in the hospital for thirty-two days and his entire convalescence in the hospital was uneventful. He was dismissed from the hospital and was instructed to use crutches until his next examination four weeks later. Three weeks after dismissal he was again seen and seemed to be getting along well except for mild pain in the left hip while walking. He was advised to have a warm bath daily and to discard his crutches when walking in his own home. He was re-examined three weeks later ten weeks after the fracture and was completely asymptomatic. Motion of the hip was normal. No further treatment was indicated and he was dismissed from our care.

Two weeks later the patient returned complaining of pain in the left knee. The examining physician felt that this was due to referred pain from the hip, as examination of the knee was normal. Doses of acetylsalicylic acid and application of heat to the left hip were advised.

The patient was not seen again until November 8, 1943, twenty four months after the fracture. His chief complaint then was pain in the left knee

and hip of eighteen months' duration. The pain had gradually become worse and for the past seven months had been severe intermittently. The pain was chiefly localized to the left hip with extension to the groin and testes and also down to the left knee. Weight bearing aggravated the pain. Weather changes had no effect on the pain but acetylsalicylic acid relieved him temporarily.

Physical examination revealed marked limitation of internal rotation of the left hip. There was no true or apparent shortening of the left lower extremity. Roentgenograms revealed that the fracture of the left greater



Fig. 284.—Left hip November 11, 1943, showing fracture of the greater trochanter with minimal displacement.

trochanter had healed. There was marked flattening of the upper third of the femoral head with osteoporosis and complete disruption of the bony trabeculae.

October 21, 1947. Postmortem examination revealed marked atherosclerosis of the abdominal aorta with ruptured aneurysm. No examination of the left hip was performed.

COMMENT

Watson-Jones stated that the blood supply to the head of the femur is derived from the capsular and ligamentum teres vessels. The capsular vessels enter the bone at the site of the capsular attachment to the femoral neck and complete their course within the bone or they run on the surface of the neck and finally enter the bone in



Fig. 233.—Left hip November 8, 1918, showing the healed fracture of the greater trochanter and marked destruction of the femoral head.

the subcapital region. These vessels supply the proximal portion of the neck and greater portion of the head of the femur. The vessels within the ligamentum teres when no an-

ticular

no an

by injury or other means the corresponding portion of the femur loses

its blood supply. The nutrient and periosteal vessels of the femoral shaft extend as high as the trochanteric region and bular portion of the neck but do not contribute to the blood supply of the head of the femur.

Wolcott¹⁴ stated that the nutrient artery from the shaft of the femur also contributes to the blood supply to the head of the femur and that the vessels from the articular capsule, ligamentum teres and nutrient artery all anastomose freely. In 80 per cent of his series of cases in which a careful anatomic study was performed the vessels from the ligamentum teres were patent even when the patient was of advanced age. In only 20 per cent of cases were these vessels obliterated.

The development of aseptic necrosis of the head of the femur can easily be understood when it occurs after subcapital and transcervical fractures,¹⁵ traumatic dislocations of the hip,¹⁶ slipped upper femoral epiphysis¹⁷ or open operations on the hip in which the capsule and ligamentum teres are damaged and interference of the blood supply results.^{18, 19, 20}

Since interference with the blood supply is recognized by many authors^{1, 2, 4-6, 11, 12} as the primary cause for aseptic necrosis, it is difficult to understand why more patients who have subcapital and transcervical fractures do not have this complication. In these fractures the femoral head acts more or less like a free bone transplant.²¹ It seems logical to assume that unless sufficient time is allowed after these fractures for new bone to replace the entire head except that supplied by the ligamentum teres, that aseptic necrosis, osteochondritis dissecans or osteo-arthritis will develop in all cases. It does not seem logical to believe that the vessels within the ligamentum teres could prevent these complications in a very high percentage of cases. This may explain the high percentage of these complications even after better methods of internal fixation and earlier weight bearing.

The facts known about aseptic necrosis depend largely on the studies of the pathologic status of the femoral head. Massive subchondral necrosis of bone and marrow of the entire epiphysis of the femoral head takes place. This is followed by disintegration and ab-

junction
cartilage usually remains smooth but may separate from the subchondral bone. The synovial membrane and capsule become thickened.

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EPIDERMMOID CYST OF THE LEFT PALM WITH DUPUYTREN'S CONTRACTURE OF THE HANDS AND RIGHT FOOT: REPORT OF CASE

HENRY W. MEYERDING AND ALFRED E. JACKSON

In 1832 Dupuytren described a contracture of the palmar fascia which produced a clawlike deformity of the hands and which likewise was found in the feet. Although a number of articles have been written about the pathology and treatment of Dupuytren's contracture of the hands only a few papers in the past fifty years have referred to this condition involving the feet. In 1897 Ledderhose concluded that the pathologic changes noted in the hands and feet affected by Dupuytren's contracture are essentially the same. In 1929 two other cases affecting the feet were described by Kamarel, Hoch and Mason. In 1934 Powers included 9 cases affecting the feet. In 1941 Hohmann described a case affecting both hands and both feet. In 1936 one of us (H.W.M.) reported a series of 978 cases of Dupuytren's contracture of the hands in 4 of which the patients had a similar involvement of the feet. Meyerding, Black and Broders, in 1941 in their study of the etiology and pathology of Dupuytren's contracture included 1 case in which the condition involved the feet. Horwitz in 1942 included a photomicrograph of a specimen removed from a possible Dupuytren's contracture of the foot. In 1948 Luck reported a series of 14 cases of Dupuytren's contracture of the foot. In a recent study of more than 800 cases of Dupuytren's contracture of the hands Meyerding and Shellito found 23 cases in which the patient had involvement of one or both feet.

Although only a few cases have been reported we feel that the condition is not as rare as the literature might indicate. The possibility of involvement of the feet should always be suspected when the patient has a Dupuytren's contracture of the hands although it is possible to have the condition limited to the feet as was reported by Powers. Symptoms may be entirely lacking, the patient may complain of moderate pain or aching, or a "lump" in the arch of the foot may cause concern. Inspection and palpation of the feet may reveal a thickening of the medial portion of the plantar aponeurosis with nodular masses on its surface, which may be adherent to the skin. Pes cavus with hammer toe deformity could result from long-standing Dupuytren's contracture but we have not observed this degree of deformity.

The pathologic picture is best explained on the basis of a chronic inflammatory process. The condition involves primarily the plantar fascia, subcutaneous areolar tissue and the skin. The possibility of an erroneous diagnosis of fibrosarcoma must be borne in mind, as illustrated in the case that we are reporting here.

REPORT OF CASE

A housewife, 58 years of age, was seen at the Clinic on October 21, 1948. She complained of tumor masses in the palms of the hands and sole of the right foot of about seven years duration. She had noticed lumps in the palms of the hands in the region of the fourth metacarpophalangeal joints. The lumps gradually had become larger with increasing bilateral flexion deformity of the fourth and fifth fingers. She stated that operation had been performed but the deformity had recurred with some numbness of the fingers that had been operated on. For the past few months the patient had noticed a similar swelling of the sole of the right foot. The family history revealed that her father had died of "leukemia" at the age of 33 years. Her mother had died at "childbirth" at 34 years of age. One son had died of acute leukemia at the age of 16 years. Her husband and three daughters were living and well. In

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veloped a depression state and was admitted to a sanatorium. She had improved during the last year but continued to be irritable and nervous.

The results of physical examination were essentially negative except for

— — — — — large lumps on the 4 and 5 feet

passed beyond this angle on passive motion.

The right hand (Fig. 256b) revealed dimpled thickened adherent skin over the distal palmar crease and the fourth and fifth fingers could not be extended fully on active motion. The dorsal view of the two hands are shown in figure 256c and d.

Examination of the right foot (Fig. 257) revealed a mass in the medial portion of the longitudinal arch with slight contracture of the plantar fascia. The examination of the left foot did not reveal anything abnormal.

The laboratory tests revealed normal urinalysis, hemoglobin, leukocyte count and flocculation reaction for syphilis; the basal metabolic rate was +17 per cent. Roentgenograms of the thorax were negative. Those of the left hand were negative for involvement of bone but showed a flexion deformity of the

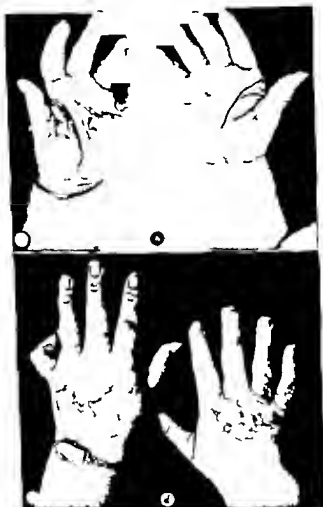


Fig 226—*a*, Left hand postoperatively showing epidermoid cyst as a recurring Dupuytren's contracture, producing flexion deformity of the fingers, *b*, right hand showing wrinkling at the distal palmar crease with a mild flexion deformity of the fifth finger and *c*, dorsal view of hands.

fifth finger and a circumscribed soft tissue mass on the palmar aspect of the distal halves of the fourth and fifth metacarpal bones.

We made a diagnosis of Dupuytren's contracture of both hands and the

right foot and sebaceous cyst of the palm of the left hand. On October 28, 1942, with the patient under infra-orbital sodium pentothal anesthesia, the palmar fascia of the left hand was excised, two incisions being made. After this procedure had been done the fifth finger could be fully extended. There was a large epidermoid cyst (keratinoma) containing cheesy material in the scar of the previous operation. The cyst, which measured 1 inch (about 2 cm.) in diameter, was excised. A subcutaneous excision of the palmar fascia was



Fig. 237.—Right foot showing tumor like mass in the medial portion of the longitudinal arch.

splints were applied to both hands and forearms to maintain the fingers in extension.

There was a large firm fibrous tumor like mass in the arch of the right foot which was excised and found to be the result of Dupuytren's contracture causing a thickening of the plantar fascia.

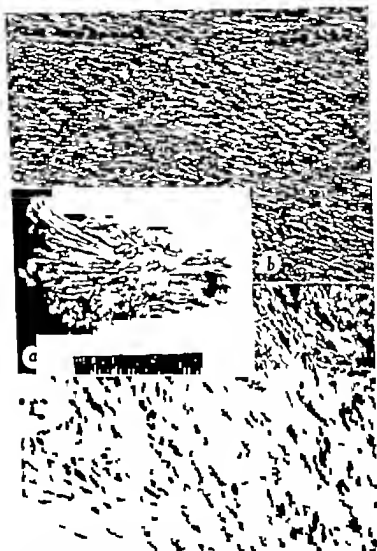


Fig. 229—*a*, Gross specimen removed from the right foot showing strands of thickened fibrous tissue involving the plaster facem. *b*, tissue from the fibrous mass removed from the right foot. Each shows the type of cellular structure ($\times 180$) being proliferating cellular area in tissue from right foot, each area have been mistaken for fibrostroma on macroscopic examination ($\times 180$)

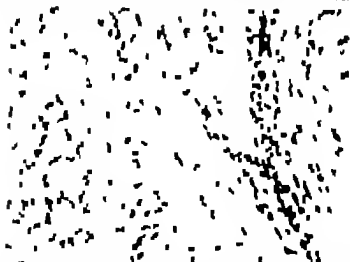
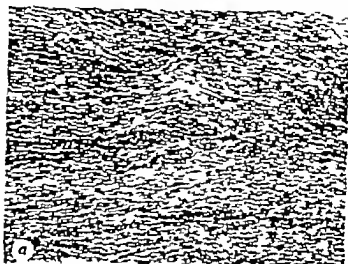


Fig. 220—*a*, Tissue removed from palmar fascia of left hand, which shows fairly cellular fibrosis in which there are no nodular figures ($\times 90$). *b*, higher magnification of same ($\times 220$).

On the seventh postoperative day the splints were removed and the incisions were found to be healed. The splints were used approximately ten days.



Fig. 290 —a, Tissue from palmar fascia of right hand, which shows fairly cellular fibrous free of mitotic figures ($\times 90$) b, higher magnification of one of the cellular areas of same ($\times 290$)

The gross and microscopic examination of the specimens showed the following findings:

Right foot—Macroscopically (Fig. 295a), a thickened, fibrous, nodular

hard, grayish mass, 5 in 3 by 5 cm in obliq the plantar fascia was observed. Microscopic examination of the tissue showed "fibrous inflammatory tissue, section of which under magnification $\times 150$ showed increased cellular area (Fig. 228b) magnification $\times 250$ shows benign proliferative areas of fibrotic tissue (Fig. 228c) which has been mistaken for fibrosarcoma in some instances.

Left hand—The epidermoid cyst located in the postoperative scar was 1.5 cm in diameter contained a soft cheese-like material and was surrounded by regions of foreign body giant cell reaction. The Dupuytren's contracture tissue was reported as "fibrous inflammatory" (Fig. 229a and b).

Right hand—Microscopic examination of the tissue removed showed "fibrous inflammatory tissue" involving the palmar fascia (Fig. 230a and b).

On the sixteenth postoperative day the patient was dismissed from the hospital after an uneventful convalescence. She returned home with instructions regarding exercises to maintain motion and extension. Her physician wrote to us two years after the operation, stating that his examination at that time revealed full function of the right hand. The left 5th finger had some motion, but a flexion contracture of 45 degrees at the proximal interphalangeal joint. The right foot was entirely normal and asymptomatic.

COMMENT

This case illustrates complications which may arise after surgical treatment for Dupuytren's contracture. The deformity recurred with numbness of the fingers, an epidermoid cyst developed suggestive of tumor (fibrosarcoma), an involvement of the plantar fascia of the right foot apparently had been unrecognized. The surgical relief of such cases of Dupuytren's contracture in which the patient has had operation previously always presents a difficult problem. After excision of the contracted and thickened palmar fascia, it is advisable to have the fingers splinted in extension until the incisions are healed. Whenever possible after the splints have been removed, a period of at least several weeks of physical therapy and supervision by the surgeon is advisable in an effort to gain maximal function of the hand.

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PYLORIC STENOSIS CAUSED BY INGESTION OF CORROSIVE SUBSTANCES REPORT OF CASE

HOWARD A. GRAY AND CHESTER L. HOLMES

THE ingestion of corrosive substances is not a rare occurrence since nearly every practitioner has directed the immediate or late treatment of some victim of corrosive injury of the alimentary tract. Corrosive substances may be ingested accidentally or taken with suicidal intent. The esophagoscopist, particularly, has been concerned with this type of injury because the damage to the esophagus frequently causes cicatricial stenosis of varying degree and extent. Most injuries of this type are due to the accidental swallowing of lye. The late effects of the ingestion of lye and similar caustics on the esophagus are well known.

There are other dangerous corrosives that are ingested less frequently than lye and similar caustics. The late effects of ingestion of these corrosives are not so generally known as are the late effects of the ingestion of lye and similar caustics. This is true for a number of reasons. Some of these are quite clear while others are not so definite. For instance, a large number of cases of ingestion of such corrosives are not reported because death ensues very shortly and no information has been gained as to what the late effects, if any, would have been. It is not so evident why of 150 reported cases in which pyloric stenosis followed ingestion of some corrosive only 11 were reported by American authors. It is the purpose of this report to review the literature on this subject briefly as to etiologic agents involved and methods of treatment employed and to report 1 case in which the patient was observed by us.

INCIDENCE

Probably the first report of a case in which pyloric stenosis followed the ingestion of a corrosive substance (sulfuric acid) was made by Robert in 1828. In this case the patient died nine weeks after ingestion of the sulfuric acid. Necropsy revealed the true nature of the obstruction. The most commonly reported corrosive agent which has eventuated in pyloric obstruction is hydrochloric acid. 12-44. 28-47. 29-34. 38-44. Sulfuric acid has caused pyloric obstruction in an appreciable number of cases. 4, 7, 8, 29, 38, 41, 42, 43. Since it appears

to be more readily available than hydrochloric acid it is ingested more frequently than is the latter acid. As pointed out by Elzecher the number of persons who die of perforation, gangrene and collapse soon after they have ingested sulfuric acid is significantly larger than is the number of persons who die of similar causes soon after the ingestion of hydrochloric acid. As a result, comparatively few people who ingest sulfuric acid live long enough for gastric and pyloric sequelae to develop. Nitric acid,^{1 2 3 4 5} trichloroacetic acid,⁶ carbolic acid⁷ and acids of unknown formula^{2-4 7 10 11 12} have been reported to have caused pyloric obstruction.

In their review of the literature Quénu and Petit^{13 14} found reports of 94 cases in which ingestion of corrosive substances had caused pyloric obstruction. In 35 of the 94 cases, the patients were treated surgically; in the remaining 59 cases, the pyloric obstruction was found at necropsy. In 52 of the 59 cases in which the obstruction was discovered at necropsy the lesion was due to ingestion of acids. In the 5 cases, it was due to the ingestion of caustics. Zinc chloride was the cause of the obstruction in 1 case while copper sulfate was the cause of the lesion in the other case. In 10 or approximately 20 per cent, of the 52 cases in which the gastric and pyloric scarring was due to ingestion of acids necropsy also disclosed esophageal strictures of some degree.

Orator found that esophageal stricture was present in 7 or approximately 20 per cent, of 34 cases in which pyloric stenosis occurred after the ingestion of an acid. Since the review by Quénu and Petit, 30 cases in which pyloric stenosis has been caused by the ingestion of an acid have been reported in the literature. Concomitant esophageal stenosis was present in only 2 or 6.5 per cent, of these cases.

Other corrosive substances which have been reported to have caused pyloric stenosis are potassium hydroxide^{1 17 18 19 20 21 22} and formaldehyde.²³ In 5 of the cases reviewed by Quénu and Petit, the pyloric scarring was due to the ingestion of potassium hydroxide. It is interesting to note that esophageal strictures were present in all of these cases. Since the publication of the review by Quénu and Petit, 14 cases in which pyloric stenosis was caused by a caustic such as potassium hydroxide have been reported in the literature. Concomitant esophageal stenosis was present in 10 or approximately 70 per cent, of these cases.^{4 14 17 18 20 21 22}

Hendall reviewed 116 cases in which esophageal stricture was caused

by the ingestion of lye. He found that pyloric stenosis was present in 20 per cent of these cases.

ETIOLOGY AND PATHOLOGY

Pyloric stenosis or antral stenosis which follows the ingestion of a corrosive substance is due to the strongly irritative nature of the erodent which causes a coagulative necrosis of the surface epithelium and submucosal tissues. Blood vessels and lymphatics are destroyed and the tissues are left more vulnerable to the continued exposure to the irritant. This process may lead to immediate perforation or to perforation after some extrinsic or intrinsic pressure such as that caused by coughing or vomiting, if the corrosive is concentrated, if exposure to its coagulative action is prolonged or if dilution and neutralization are delayed.

Alkalies, most notably potassium hydroxide (according to Delore and Arnaud) have a deep coagulating effect upon all tissues. They burn the esophagus as they are swallowed. Since they are quickly neutralized by the acid gastric contents they do not cause extensive gastric damage as frequently as acids do.

Acids, on the other hand, seem to have a more superficial action on the esophagus but on reaching the delicate columnar epithelium of the stomach they cause considerably more damage. Since dilution is an important factor in rendering the corrosive innocuous, the ingestion of a corrosive on an empty stomach will cause more serious injury than will the ingestion of a similar corrosive on a full stomach. Furthermore, the stronger the concentration of the irritant, the more likely it is to be ejected quickly while weaker solutions may be tolerated and the duration of the exposure dangerously prolonged.

Any part of the stomach may be injured but the most frequent site of the scarring is the pylorus and the pyloric antrum. This is satisfactorily explained by the work of Grützner, Cohnheim and Waldeyer. Grützner demonstrated by means of various colored fluids that stratification and storage occurred in the fundus. Cohnheim demonstrated that ingested fluid appeared unchanged in the duodenum. It remained for Waldeyer to develop the concept of a common pathway for rapid transit of fluids from the esophagus to the pylorus without the admixture of food and a pathway for well triturated food from the stomach to the duodenum. This pathway he termed the "magenstrasse."

Against this background it is not difficult to visualize the transit of the corrosive substance along the magenstrasse until it reaches the

pylorus and causes a strong spasm which prolongs the exposure time markedly. This spasm will further delay the process of normal buffering and dilution by the contents of the stomach. Samaya expressed the opinion that the tetanic contractions are of the utmost importance in concentrating the effect of the irritant at the pylorus.

More recently Testa added baryum to a caustic and observed the progress of the mixture roentgenoscopically. He found that this compound flowed along the lesser curvature to the pyloric antrum where severe spasms occurred for a variable length of time.

The pathologic changes are extremely variable in extent although the process is similar wherever found. Aside from the early acute pathologic changes, such as eversion of the entire alimentary tract from lips to duodenum which will not be considered, the late complications are based on the cicatricial contraction of the fibrous tissue, produced by the early damage, and on the normal attempt of the body to repair this injury.

In cases in which the ingestion of a corrosive causes pyloric obstruction, dehydration and acidosis, the pathologic changes in the stomach will vary widely. The lumen of the stomach may be obstructed almost entirely and the tissues may be firm, rough and nodular and extremely contracted. The entire stomach may be diffusely affected but the greater curvature, fundus and cardia will be relatively less scarred than the lesser curvature, pyloric antrum and pylorus. In most cases, however, the only change is scarring of the antrum or of the pyloric ring. Hour-glass deformity of the stomach and other intermediate degrees of scarring are seen occasionally.

If seen relatively recently (four to ten weeks) after the ingestion of the corrosive substance, the tissues will be found to be indurated

mucosa, and muscularis mucosa is seen. Polymorphonuclear leucocytes gradually disappear and a round cell infiltration characteristic of chronic inflammation, takes place. Repair of the surface epithelium may be expected to occur in time, but the rugae and gastric glands usually are destroyed and the thin layer of regenerated epithelium is likely to undergo ulceration.

Putman reported a case in which the entire columnar epithelial lining had been destroyed and the stomach was lined by a squamous type of epithelium which the pathologist interpreted as a downgrowth of epithelium from the esophagus. Broders expressed the opinion that

metaplasia of the gastric epithelium is a more logical explanation for this change.

More diffuse involvement of the layers of the wall of the stomach destroys the plexuses of nerves and this destruction plus fibrosis of the remaining musculature interferes with the motility of the stomach. Van Gieson's stain will distinguish fibrous tissue from normal muscle fibers.

SYMPTOMS

Immediately after a corrosive substance has been ingested severe local burning of the lips, mouth and pharynx will be noted and sub-sternal pain, nausea and vomiting will occur. The vomiting is likely to be severe and protracted. If it does not occur immediately after the ingestion of a corrosive substance it will occur a short time later. The vomitus has a characteristic foul odor and is of a dark color owing to the presence of blood. It may contain moderately large pieces of gastric mucosa. For several days, coffee or tea may be the only article of diet that can be retained in the stomach. These symptoms usually continue for twenty-four to forty-eight hours. The patient may feel better at the end of this period but severe anorexia usually is present for one or two weeks.

In from ten days to two or three weeks after the ingestion of the corrosive substance many patients will have recovered sufficiently to be dismissed from the hospital. In some cases, pyloric stenosis will develop in four to six weeks after the patients have been dismissed from the hospital. In such cases, the patients will begin to vomit and will lose weight rapidly. They will become dehydrated and alkalosis will develop.

In cases in which lye has been ingested, the patients may require treatment for dysphagia before pyloric stenosis develops. Treatment of both of these complications was necessary in the case reported by Czerny and Rundfleisch. Six months after gastrostomy had been performed for esophageal stricture the opening in the stomach was closed and pyloroplasty was performed for pyloric obstruction. Vinson and Hartman reported a case in which the esophageal stenosis was treated successfully although the guide thread became matted in the stomach and caused a partial pyloric obstruction to become complete. In 2 cases reported by Galdin and Pop a pyloric stricture developed three years and six years respectively after an esophageal stricture had been treated successfully. Dujardin-Beaumetz reported a case in which pyloric stenosis developed six years after the ingestion of a

corrosive substance and Ortmann reported a case in which this complication developed five years after the accident. In the case reported by Dujardin-Beaumetz, the patient died.

In an occasional case a posterior gastro-enterostomy has been performed for pyloric stenosis and a gastrostomy has been performed simultaneously to facilitate the treatment of an esophageal stricture.¹⁰

DIAGNOSIS

The diagnosis of pyloric obstruction is not difficult, particularly if one is aware that corrosives especially acid have a tendency to produce intense scarring in the pyloric region. The history of ingestion of a corrosive substance should cause one to suspect that such scarring possibly may be present. If the patient begins to vomit retained food week or two after he apparently has recovered from the immediate effects of the corrosive substance it is reasonable to assume that pyloric scarring probably is present.

diffuse or even scattered over the viscus

Röntgenologic examination will confirm the diagnosis of pyloric obstruction and secondary gastric dilatation if present, although the thickening of the pyloric antrum, absence of peristalsis and absence of a normal mucosal pattern may suggest the diagnosis of carcinoma unless the history accompanies the request for roentgenologic ex-

amination by

Y
17

¹⁰ after the ingestion of an erodent, the diagnosis after roentgenologic examination may be obstruction due to a neoplastic growth or possibly an ulcer if the patient fails to mention the incident because he does not realize the close relationship between the ingestion of the erodent and the vomiting which develops several years later. Operation, of course, will prove that the pyloric stenosis is benign. The true cause of the stenosis may be misinterpreted if a well-localized area of scarring is encountered.

TREATMENT

the physical condition of the patient, and the ability and judgment of the surgeon.

When the patient is seen early after the ingestion of an erodent substance medical measures should suffice as the patient is not assured of living long enough for stenosis to develop and a major surgical operation is not indicated. If vomiting persists and dehydration and malnutrition develop in spite of medical measures, operation may become necessary. In case it does, a jejunostomy seems to be the operation of choice. This permits fluids and food to be administered while the local acute inflammation is given an opportunity to subside sufficiently to permit the performance of a resection or another elective procedure. Once stenosis of the pylorus has developed definitive operation is obligatory and usually possible although the residual acute or subacute inflammation may make the operation difficult.

The first recommended procedure for gastric lesions of this type was that which was described by Loreta in 1884. He advised digital dilatation of the stricture but found, as did White and Lane, that the stenosis was almost certain to recur. In their case which was reviewed by Quénou and Petit, the patient died the third day after the second operation of this type. Other potent dangers of this procedure are rupture, hemorrhage and infection. Senn used this procedure but felt that these dangers plus the rather good results obtained with the pyloroplasty of Heineke and Mikulicz made the further use of dilatation unjustifiable. Czerny and Rindfleisch and Arena also favored pyloroplasty wherever possible.

Gastro-enterostomy has been preferred by the majority of surgeons confronted with this condition. Certain considerations in the light of experience with gastro-enterostomy in general make this a debatable point.

Partial gastrectomy has been employed only three times in similar cases reported in the literature. The case which we shall report is the fourth case in which partial gastrectomy has been performed for pyloric stenosis which followed ingestion of a corrosive substance. In none of these cases has the rationale for this particular operation been presented. We wish to clarify this situation somewhat by a brief

consideration of the problems involved in definitive therapy of pyloric stenosis irrespective of its cause



Fig. 231.—Esophagogram showing marked dilatation of the stomach, complete obstruction of the pylorus and retention of large amount of secretions

REPORT OF CASE

A man, aged 33 years, came to the Clinic on June 29, 1948, because of
weeks. On May 14,
was he had symptoms
he had drunk a pint of

milk and had gone to a hospital. He had begun to vomit while he was in the hospital and the vomiting had been severe for several days. He had been dismissed from the hospital in one week, and a bland ulcer diet, including milk and cream, had been prescribed. After he had been dismissed from the hospital, he occasionally had vomited a small amount of blood. Three weeks later he had begun to vomit nearly everything that he ate; the vomiting usually occurred about an hour after he had eaten. He had lost 80 pound (15.6 kg.)



Fig. 194.—Curved portion of stomach showing ulceration of mucosa and structure of the pylorus.

When the patient came to the Clinic he did not have any pain. His temperature was 97.4°F . His blood pressure was 110 mm. of mercury systolic and 70 mm. diastolic. Percussion did not disclose any evidence of dilatation of the stomach. Roentgenologic examination of the thorax did not reveal any abnormality and examination of the esophagus did not disclose any evidence of stenosis. Roentgenographic examination of the stomach disclosed marked dilatation, complete obstruction of the outlet, and a large amount of retained secretion (Fig. 191).

A diagnosis of pyloric obstruction was made and the patient was prepared



Fig 293 —a, Section of pyloric region showing elevation, thickening and edema (hematoxylin and eosin, $\times 8$) b, Deposits of fibrous tissue in the submucosa and between muscle bundles (van Gieson's stain, $\times 8$)

for operation by gastric lavage and by the parenteral administration of fluids. Operation was performed by one of us (H. K. G.) on July 2. The patient was anesthetized with a mixture of nitrous oxide, oxygen and ether. An intra-tracheal tube was inserted to insure an adequate airway. A primary right upper rectus incision was made and the stomach was exposed. This revealed rather marked thickening and obvious mechanical obstruction of the pylorus. The stomach was dilated; its walls were thick and the serosal surface was rather markedly congested and had an edematous appearance. There was a moderate number of adhesions in the abdomen, particularly between the transverse colon and a rather redundant ascending colon, which was angulated and had encroached upon the vessels of the first portion of the jejunum. The colon was freed and a partial gastrectomy was performed by removing approximately half of the stomach and a small rim of the duodenum. Gastro-intestinal continuity was restored by means of an anterior Polya type of anastomosis which was chosen because of the presence of a rather short, thick, transverse mesocolon. Exploration of the remainder of the abdomen did not reveal any other abnormality.

Gross examination of the portion of the stomach that was removed at operation revealed ulceration of the mucosa in the pyloric region and a stricture of the pylorus (Fig. 297). Microscopic examination disclosed ulceration of the mucosa in the prepyloric region (Fig. 298a) and the presence of fibrous tissue in the submucosa and between the bundles of muscle (Fig. 298b).

The convalescence was uneventful for four days. During this time there was no evidence of gastric retention. The patient was to get out of bed on the fourth day. On the fifth day the temperature rose to 104° F. and the patient complained of some malaise and mild distress in the right lower quadrant of the abdomen. The patient was not permitted to take anything by mouth and he was instructed to remain in bed. The presence of a slight leak at the site of closure of the duodenal stump was suspected. The administration of penicillin and sulfacholine was started. The temperature did not rise further and it returned to normal on the tenth day after the operation. A gastro-enterostomy type of diet was prescribed and this was supplemented gradually until a full diet was being taken. The patient was dismissed from the hospital on the nineteenth postoperative day and from the Clinic the twenty-third postoperative day.

The patient's physical condition continued to improve after he returned to his home. His weight slowly returned to normal and the patient has informed us that his appetite is excellent.

COMMENT

In the treatment of pyloric stenosis that follows the ingestion of corrosive substances, the ultimate goal is, of course, to restore the normal passage of food from the stomach to the small intestine where the later stages of digestion are completed and to restore normal

nutrition and normal fluid and electrolyte balance. This can be accomplished satisfactorily by pyloroplasty, gastro-enterostomy or partial gastrectomy.

The various types of pyloroplasty that have been described by Hemeke, Mikulicz, Finney and Judd may find a place in the treatment of structure of the pylorus. This will depend on the local condition of the tissues and the extent of the pathologic process. This type of operation may be entirely adequate in cases of localized scarring of anterior pyloric wall. In cases in which the scarring is more extensive the necessity of suturing through scarred and indurated tissues, even in a portion of the incision, would render its use less desirable.

Gastro-enterostomy may have a place in the treatment of this condition but its use also is subject to certain disadvantages. Among these are the problems of accomplishing a good anastomosis in the presence of diseased gastric tissues. The advisability of leaving a scarred contracted stomach with little or no motility and with a chronic inflammation and ulceration of the mucosa at or distal to the site of anastomosis is to say the least, questionable. We have no positive information as to the effect of extensive chemical irritation in predisposing to the development of a malignant lesion but we are satisfied that malignant changes occur on other epithelial surfaces as a result of somewhat similar irritating influences. In addition to numerous examples of chronic ulceration and gastritis we have observed one example of what was in all probability an extensive metaplasia of the entire gastric lining to a squamous type of epithelium. The final judgment as to the significance of this metaplastic change in the stomach or elsewhere, for example in the cervix uteri, has not been determined, but we are confident it is a significant departure from the normal.

One other important disadvantage of gastro-enterostomy is the tendency for stomal ulcer to develop after this operation has been performed. It cannot be assumed that such an ulcer will develop only in cases in which there is a characteristic ulcer diathesis. In cases in

peptic ulcer. In such cases, it must be assumed that the gastro-enterostomy was performed on the basis of an erroneous diagnosis. The development of a gastroduodenal ulcer in such cases is evidence that a definite ulcer diathesis is not an absolute requisite for the development

of gastrojejunitis or a stomal ulcer. Every effort should be made to prevent the development of a gastrojejunal ulcer which is most likely to occur in cases in which the patients are young and have a nervous temperament. It is far more common among males than it is among females. In some cases in which scarring of the gastric mucosa has resulted from ingestion of a corrosive substance the scarring has a tendency to reduce the acidity of the gastric contents. The effect of this reduction of acidity on the development of a gastrojejunal ulcer cannot be stated. Theoretically it may offer some protection against the development of such an ulcer.

Partial gastrectomy was performed in this case because it was believed that it would achieve the most satisfactory functional result and would protect the patient as well as possible against the common complication of gastro-enteric anastomosis. We have not been able to find a report of a case in which the gastric injury was extensive enough to require total gastrectomy. In cases in which the injury of the stomach is so extensive the patients undoubtedly do not withstand the initial shock and the subsequent toxemia.

It may be argued that, since partial gastrectomy is a more extensive procedure than gastro-enterostomy it is less applicable than gastro-enterostomy but for a competent surgeon, we believe that it is the operation of choice in cases in which the patients are young.

SUMMARY

This paper is based on the report of a case in which pyloric stenosis developed about a month after the ingestion of $1\frac{1}{2}$ ounces (45 cc.) of sulfuric acid. A review of the literature has disclosed reports of 159 other cases in which pyloric stenosis has followed the ingestion of a corrosive substance.

The ingestion of caustic alkalis injures the esophagus and frequently causes cicatricial stenosis of this organ. Although corrosive alkalis usually are quickly neutralized after they enter the stomach gastric or pyloric stenosis occurs in about 20 per cent of cases in which these corrosives are ingested.

The effect of ingested acids is noted generally as a pyloric or antral stenosis. This usually causes symptoms in about four to six weeks, although the literature contains reports of several cases in which there was no evidence of pyloric obstruction until five or six years after the ingestion of an acid. Approximately 20 per cent of patients with pyloric stenosis due to ingestion of a corrosive acid also will have an esophageal stricture.

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EOSINOPHILIC GRANULOMA OF THE SKULL REPORT OF FOUR CASES WITH FIVE-YEAR FOLLOW UP

GEORGE S. BAKER AND ROBERT G. FISHER

In the past decade a comparatively new clinical entity has been described under the title of "eosinophilic granuloma of bone." This condition was not distinguished as a separate clinical entity until 1940.

As every general practitioner knows it is important, when an osteolytic lesion of the skull without any other findings is discovered to know whether the lesion is benign or malignant. This paper it is hoped, will be of some value in this respect. The paper includes a follow-up study of five years' duration, of 4 men who were seen as patients in the United States Army. In addition a discussion of the entity "eosinophilic granuloma of bone" and a review of the literature will be presented in some detail.

HISTORICAL FACTORS

Finn in 1929 described a myeloma of the frontal bone in a boy 13 years old. This myeloma was a circumscribed lesion with a cellular picture predominantly that of eosinophilic leukocytes. Mignon described the same picture in 1930 in a child brought to the Innabrook Clinic with a "tumor" in the left frontal bone. Schaller² described two cases in which he gave fundamental recognition to a new clinical entity but he subtitled his paper "Osteomyelitis with an eosinophilic reaction."

Three groups of authors in this country in 1940 independently described "eosinophilic granuloma." Otani and Ehrlich referred to the condition as "solitary granuloma of bone" which simulated a primary neoplasm. In one case there was a lesion of a rib in another the scapula was involved. These authors were impressed with a single painful swollen lesion and they believed trauma contributed to the development of the tumor. The rib involved in their case had a thickened periosteum the marrow and cortex were destroyed. Microscopically large pale cells, leukocytes multinucleated giant cells, destruction and repair products were seen. In the same journal two months later Lichtenstein and Jaffe published a paper called "Eosinophilic granuloma of bone" and in another journal during the same month Hatch³ entitled his paper "Eosinophilic granuloma of bone."

In the case of Lichtenstein and Jaffe the lesions were wedge and the bone was replaced by soft yellowish or brownish tissue. These lesions started in the medullary cavity, crested and expanded the cavity perforating the cortex and the bone site affected. The lesion in these cases afflicted children and young adult persons. Hatcher had 3 children in his series in which there was involvement of the long bones. The lesion in his case exhibited central rarefaction, cortical erosion and marked pericortical thickening causing him to make a preoperative diagnosis of "sarcoma."

Farber followed the evolution of 10 children in whom there were granuloma involving not only flat bone but long bones as well. The follow-up period varied from three to ten years. Microscopically areas of focal necrosis with large mononuclear phagocytes dominated the picture. The value for blood cholesterol was normal in all patients. It is of interest to note that Farber's patient did well after roentgen therapy or curettage, some of the lesions healed spontaneously.

Additional cases then appeared in the literature. Hase, Thurman and Cross and Jacob summarized the literature up to 1942 by stating that 16 cases had been reported and that all but 3 of the patients were younger than twenty-one years. Of the 16 cases, 11 consisted of lesions of the skull. Only 4 patients presented a history of trauma. Green and Farber added an important point to the original report of Farber. They wrote that if there is any question of the lesions being other than eosinophilic granuloma, the possibility of visceral lesions should be borne in mind. They published this paper with the idea in mind that the differential diagnosis between eosinophilic granuloma and Histiocytosis-Schüller-Christian disease is difficult indeed.

Additional reports of cases appeared in 1943. Schaller²⁴ in his series presented 1 case of eosinophilic granu-

re not mentioned the wall and floor of exit of the facial

and acoustic nerves. The patient had peripheral facial palsy with headache, giddiness and vomiting. He also had tinnitus, vertigo and nystagmoid jerks. Since this patient had deep pain in the ear, Osborne and associates presumed that the geniculate ganglion was involved. Their assumptions were substantiated partially by sub-occlusion of the symptoms and signs referable to the lesions of the facial and acoustic nerves after roentgen-ray therapy had been instituted. Multiple lesions of the skull and mandible were reported by Balman

and Darlington. Involvement of the right orbital roof by the lesion under consideration has been reported by Wheeler so that this particular feature may be confused with one of the triad of signs found in Hand-Schüller-Christian disease. In 1946 Dundon and others summarized the known literature on eosinophilic granuloma with a presentation of 53 cases. In 36 of these cases the patients were males; most of them were less than 20 years old. In 36 of the 53 cases the lesions were solitary. 36 per cent of these solitary lesions were situated in the skull. In 10 cases in which lesions were multiple, 8 lesions appeared in the skull. This represented a percentage of 11 in respect to the total number of lesions.

Clinically, pain, tenderness and swelling of the soft tissues were presented in these cases. In some cases, muscular spasm and atrophy were present. Fever, anorexia, fatigability, headache and loss of weight were reported. In some the leukocyte count, the eosinophil count and sedimentation rate were elevated.

Röntgenograms showed a round, oval or irregularly shaped area of decreased density demarcated from adjacent normal bone. There was no osteoporosis surrounding the bone. Dundon and associates described the early lesion as being cystic and hemorrhagic with soft, brownish red material. The lesion later became pale yellow. The macroscopic picture varied in different stages, with foci of necrosis and hemorrhage appearing early. The cellular picture included eosinophilic leukocytes, myelocytes, larger histiocytes, lymphocytes, plasma cells, neutrophilic leukocytes, multinucleated giant cells and foam cells which were mononuclear histiocytes. The presence of foam cells has caused some authors to relate eosinophilic granuloma to Hand-Schüller-Christian disease and to Letterer-Siwe disease. Dundon and associates felt that the prognosis is good and that biopsy usually is indicated. The roentgenologic program they suggested consists of the administration of 400 to 500 and 1,200 to 1,800 r measured in air.

Hamilton and associates reported 9 cases of eosinophilic granuloma in all of which the lesion was confirmed pathologically by the Army Institute of Pathology. In these cases neither visceral manifestations nor pathologic factors appeared. This report has served as an introductory paper to our follow-up report on 4 of the 9 cases. Hamilton and co-workers presented the features of an osteolytic lesion which is benign and can be treated adequately by roentgen ray therapy. In some of these cases biopsy was done to establish the diagnosis.

In a comment of the *Journal of the American Medical Association*⁴

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Additional report of case appeared in 1950. Schauer in his series, presented 1 case of eosinophilic granu-

N

and acoustic nerves. The patient had peripheral neuritis, headache, giddiness and vomiting. He also had tinnitus, vertigo and nystagmoid jerking. Since the patient had deep pain in the ear Osborne and associates presumed that the geniculate ganglion was involved. Their assumption were substantiated partially by subsidence of the symptoms and signs referable to the lesions of the facial and acoustic nerves after roentgen-ray therapy had been instituted. Multiple lesions of the skull and mandible were reported by Falman

and Darlington. Involvement of the right orbital roof by the lesion under consideration has been reported by Wheeler so that this particular feature may be confused with one of the triad of signs found in Hand-Schüller-Christian disease. In 1946 Dundon and others summarized the known literature on eosinophilic granuloma with a presentation of 53 cases. In 36 of these cases the patients were males, most of them were less than 20 years old. In 36 of the 53 cases the lesions were solitary. 36 per cent of these solitary lesions were situated in the skull. In 10 cases in which lesions were multiple, 8 lesions appeared in the skull. This represented a percentage of 11 in respect to the total number of lesions.

Clinically pain, tenderness and swelling of the soft tissues were present in these cases. In some cases, muscular spasm and atrophy were present. Fever, anorexia, fatigability, headache and loss of weight were reported. In some the leukocyte count, the eosinophil count and sedimentation rate were elevated.

Roentgenograms showed a round, oval or irregularly shaped area of decreased density demarcated from adjacent normal bone. There was no osteoporosis surrounding the bone. Dundon and associates described the early lesion as being cystic and hemorrhagic with soft, brownish red material. The lesion later became pale yellow. The microscopic picture varied in different stages, with foci of necrosis and hemorrhage appearing early. The cellular picture included eosinophilic leukocytes, myelocytes, larger histiocytes, lymphocytes, plasma cells, neutrophilic leukocytes, multinucleated giant cells and foam cells which were mononuclear histiocytes. The presence of foam cells has caused some authors to relate eosinophilic granuloma to Hand-Schüller-Christian disease and to Letterer-Siwe disease. Dundon and associates felt that the prognosis is good and that biopsy usually is indicated. The roentgenologic program they suggested consists of the administration of 400 to 500 and 1,200 to 1,800 r. measured in air.

Hamilton and associates reported 9 cases of eosinophilic granuloma in all of which the lesion was confirmed pathologically by the Army Institute of Pathology. In these cases neither visceral manifestations nor pathologic factors appeared. This report has served as an introductory paper to our follow-up report on 4 of the 9 cases. Hamilton and co-workers presented the features of an osteolytic lesion which is benign and can be treated adequately by roentgen-ray therapy. In some of these cases biopsy was done to establish the diagnosis.

In a comment of the *Journal of the American Medical Association*,

mention is made that the lesion is self-limited and that lesions may appear at any place proximal to the wrists and ankles. No deaths were ever reported from the granulomatous process in itself.

REPORT OF CASES

CASE 1 — A white man 21 years old had symptoms of numbness and trembling of the right hand and arm in October 1943. He had had generalized convulsions, but not headache or vomiting. Weakness of the right arm was present. There was no papilledema and the cranial nerves were not involved. The reflexes were increased on the right side. Leukocytes numbered between 8,000 and 8,000 per cubic millimeter of blood, with an eosinophil proportion of between 5 and 5 per cent. The sedimentation rate (Westergren) was 9 mm. in one hour. The value for total serum protein was 7.1 gm. per 100 cc. The albumin-globulin ratio was 1.8:1. The value for blood cholesterol was 123 mg. per 100 cc. that for phosphorus was 4 mg. per 100 cc. those for calcium and phosphatase were normal. Lumbar puncture, done on November 18, 1943, disclosed a value for protein of 40 mg. per 100 cc. and for chloride, 77.8 mg. per 100 cc. A roentgenogram on October 29, 1943, of the thorax gave normal results; mediastinal calcification was seen at the left pulmonary apex. A rounded area 2.5 by 2 cm. (Fig. 294) of decreased density was found on the left parietal bone behind the coronal suture. There was no surrounding zone of increased density. The sella turcica was normal.

The clinical impression was that a single osteolytic lesion was situated in the left parietal bone. The most likely diagnoses appeared to be: metastatic lesion, pyramia, tuberculosis, vascular tumor or Boeck's sarcoid.

On this basis, left temporal parietal craniotomy was done on November 16, 1943. A circumscribed lesion 3 by 4 cm. was found in the skull near the parietal vertex. Both tables of the skull were destroyed; the area was filled with soft, grayish yellow friable tissue. Electrocautery was used to remove this material. On December 1, 1943, results of ventriculogram were found to be normal. The wound made to remove a specimen for biopsy was reopened. The lesion was found to have invaded the cortex of the brain. One convolution was everted in a circular manner in order to remove the greater portion of the lesion.

A few cells had the same process was then in a course of ten removed series of convulsions. These for the most part were Jacksonian. They involved the

right side of the body. A regime of anticonvulsant medication was prescribed. The patient eventually was discharged from the army and was sent to Veterans Administration Facility. He was discharged from the Veterans Administration Facility about three months after his admission. He had three convulsions in one day in April of 1944 when his supply of anticonvulsant agents became depleted. In November of 1944 the patient was experiencing considerable distress because of frontal headache. Despite medication, grand mal convulsions occurred about once a month. The patient ap-

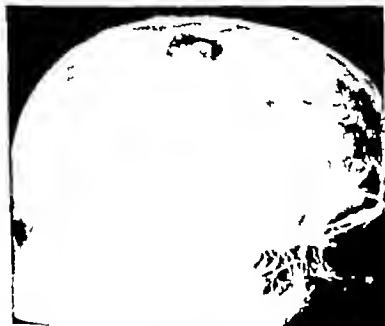


Fig. 224.—Roentgenogram showing area of decreased density with no surrounding zone of increased density in left parietal region.

parently was much depressed as a result of his condition. He attempted to

suicide disclosed nothing significant. The patient reduced his total daily intake several in oh

To the time of this report, the patient had not complained of additional attack and he was planning to re-enter college.

CASE 2—A white male 21 years old in September of 1945 noticed the onset of frontal headache with pain in the region of both eyes. He did not have



Fig 226—Low-power magnification of specimen taken for biopsy showing an extensive cellular infiltrate of mononuclear leukocytes, lymphocytes and cells with suggestive foamy cytoplasm.

convulsions, changes in mood, senses or speaking. Results of general examination of the region of the palmating cent were leukocytes ca. 3.5 mg

per 100 cc. for total proteins, 6.1 gm. per 100 cc. The basal metabolic rate was +7 the value for cholesterol was 194 mg. per 100 cc. of plasma. Reaction of the Kahn test was negative, as were results of urinalysis, except for the finding of Bence Jones protein. The bones were normal, except for the skull. A large round area of osseous destruction 2.5 cm. in diameter was seen in the left frontal bone. Both tables of bone and the diploe were involved. The margins were smooth; there was no surrounding area of increased density. The roentgenograms were compared with those made in another hospital previously; it was seen that the defect had increased considerably in three weeks. The clinical impression was that a metastatic neoplasm was present. On November 16, 1943, biopsy was performed. The lesion seemed malignant.

of the outer table. Microscopically acute and chronic granulation tissue was decreased with areas of necrosis and many multinucleated giant cells. It was decided that the process was an eosinophilic granuloma and this was confirmed by Dr. H. L. Jaffe and by the Army Institute of Pathology. After the operation there were no complications and the patient was discharged from the army. He was examined on October 14, 1947, and was found by the Veterans Administration Facility to be totally asymptomatic. The defect was approximately the same as it had been in 1943. There were no additional neurologic observations.

CASE 2—A white man 19 years old in February 1944 was walking in the barracks of his unit of the army when he fell, striking the posterior part of the skull. He did not lose consciousness, but shortly after this episode he began to have headaches in the frontal region, associated with diplopia and dizziness. He was found to have a lesion of the skull. A palpable mass was present in the left occipitoparietal region. The optic disks were choked 1 diopter bilaterally. The reaction of the Kahn test was negative as were results of urinalysis. Leukocytes ranged from 8,800 to 9,800 per cubic millimeter of blood. Differential counts gave normal results, except that on one occasion eosinophils amounted to 7 per cent. The value for hemoglobin was normal; that for cholesterol ranged from 152 to 167 mg. per 100 cc. of plasma; that for calcium was 11 mg. per 100 cc. of serum; and that for alkaline phosphatase was 7.7 Bodansky units per 100 cc. of serum. Results of a roentgenologic survey were negative except that a defect was seen in the left parietal bone. Craniotomy

developed. A course of roentgen ray therapy was started. Soon after this the soldier returned to full duty.

The lesion grossly and microscopically was similar to the others reported herein as confirmed by the Army Institute of Pathology. In November of 1944 the patient began to complain of bilateral headaches in the parietal region. He stated that his left wrist felt weaker and that it seemed to tire easily. He was experiencing arithmias limited to the left arm; they consisted of slight jerking of the forearm in flexion movement at the elbow. In May 1948 this patient was working steadily, had no convulsions, and had normal vision.

CASE 4.—A white man 37 years old was dismounting a machine gun from tank when he was struck on the top of the head by the turret of the tank. He lost consciousness for a few minutes. A lump developed at the site of the



Fig. 348.—Roentgenologic appearance of lesion about 3 cm. in diameter. Arrows indicate the osteolytic lesion.

injury and persisted for several days. Generalized headaches, blurring of

vision, and weakness of the left arm were noted. Examination disclosed a large, firm, nontender mass in the region of the left parietal bone, which was poorly to light. Results of Kahn test and of urinalysis were negative. Hemoglobin 14.0 g. per 100 cc. of blood; hematocrit 45.0 per cent; red blood cells 4,500,000 per cubic millimeter of blood; leukocytes 10,000 per cubic millimeter of blood; platelets 150,000 per cubic millimeter of blood; serum cholesterol 225 mg. per 100 cc. of plasma. Phosphorus 3.5 mg. per 100 cc. of plasma. The alkaline phosphatase of serum. On April 14, 1944,

biopsy and curettage were done. Fragments of sequestered bone were found, with an old organized clot.

The microscopic picture was that of eosinophilic granuloma. Healing of the wound occurred per primum. Postoperatively headaches disappeared from the left side of the parietal region of the skull, but began to involve the frontal region. Because of the persistent headaches the patient was discharged from the service. In November of 1944, information received from the Red Cross indicated that the man was experiencing frontal headaches lasting about one to two hours in the morning, accompanied by nausea. He claimed that his memory was poor and that he was nervous, moody and irritable. These contentions were confirmed by his wife. It was thought from a psychiatric standpoint that this man's condition was complicated by an anxiety neurosis. In May 1948 this patient was re-examined by physicians at a Veterans Facility and was found to have the same symptoms of an anxiety neurosis, but results of a neurologic examination were negative.

COMMENT

Because the nature of eosinophilic granuloma is unknown, keen academic interest in this lesion has arisen. Every general physician realizes that when he is confronted with an osteolytic lesion of the skull it is important to know whether the lesion requires surgical or roentgen-ray therapy or no treatment at all. A number of theories as to the nature of this condition have been developed recently. Frazer, in a general discussion of lipomatoses, concluded that such entities as Gaucher's disease, Niemann-Pick disease and Hand-Schüller-Christian disease all ought to be included in a heterogeneous group characterized by an excess of lipoids in the body fluid. Thannhauser and Magendanz discussed the different clinical groups of xanthomatous diseases; they believed that membranous bone lesions similar to those associated with eosinophilic granuloma may occur as part of general osseous xanthomatosis without exophthalmos and diabetes insipidus. Wallgren did not distinguish eosinophilic granu-

process or (2) it is related to Hand-Schüller-Christian disease and Letterer-Siwe disease. Farber felt that eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease all are related and that this relationship is based on a common histologic pattern: areas of focal necrosis, large mononuclear phagocytes and foam cells. Lichtenstein, in a discussion of the paper in 1941, felt that presence of foam cells is insufficient evidence on which to link Hand-Schüller

Christian disease eosinophilic granuloma and Letterer-Siwe disease Gross and Jacox stated that Hand-Schüller-Christian disease is a generalized hyperplasia, of lipoid variety of the reticulo-endothelial system. He mentioned a classic triad defects in the skull, exophthalmos and diabetes insipidus, although one feature or all features may be absent. They wrote that Hand-Schüller-Christian disease and eosinophilic granuloma have common features in that both conditions are associated with destruction and replacement of normal tissue by granulomatous tissue in which endothelial cells predominate. Eosinophilic participation occurs in both conditions. Gross and Jacox described Letterer-Siwe disease as a nonlipoid reticulo-endotheliosis which is nearly always fatal and which occurs in infants and children.

Gross and Jacox felt that eosinophilic granuloma is a type of reticulo-endotheliosis and that it is identical with Hand-Schüller-Christian disease. Mallory said that the three are variants within the same disease entity. That is, one variant is Letterer-Siwe disease, which in infancy is rapidly progressive and fatal. The second variant is a chronic serious type of condition in which there is cerebral and hypophyseal involvement this is Hand-Schüller-Christian disease. The third variant is the benign type of condition in later childhood or adult life this is eosinophilic granuloma. Jaffe and Lichtenstein¹⁰ in 1944 concluded that the three conditions actually are different clinical anatomic expressions of the same basic disturbance. They said that the three diseases are peculiar inflammatory reactions to the same as yet unknown agent of infection and that individual lesions are characterized by the presence of large numbers of histiocytes. They also said that eosinophilic granuloma can undergo spontaneous healing.

DISCUSSION

Eosinophilic granuloma does not undergo lipoplastic conversion of histiocytes, with eventual fibrosis. They believed that the lesions may undergo spontaneous resolution and that little is known about the early skeletal lesions of Hand-Schüller-Christian disease which may resemble eosinophilic granuloma. They wrote that there is enough difference between the three clinical patterns to permit the distinctions to be retained.

TREATMENT

In the past, there has been considerable variation in the methods of treatment of eosinophilic granuloma. As has been said, the condition

was not described as such until 1940 so that methods employed in the past were based on the assumption that the process was a type of osteomyelitis. Hence various agents were used to treat the disease as an infectious process would be treated. As Farber pointed out these lesions have been treated surgically with curettage or roentgenologically or they have not been treated at all on the assumption that they would undergo spontaneous resolution.

If it is possible to be certain of the diagnosis of eosinophilic granuloma biopsy may not be necessary depending on the course of the disease. If a patient presents himself with an osteolytic lesion of the skull in which there is a palpable swelling and a defect in the skull and no other manifestations of systemic or generalised disease, then consideration of eosinophilic granuloma in the differential diagnosis would be justified. In the experience of one of us (G S B) the lesion undergoes better repair in time if at the time of biopsy curettage is not done and the lesion is treated merely by roentgen-ray therapy. This is due to better bony proliferation from a spicular matrix. Because of the nature of the expanding destructive process of eosinophilic granuloma, it is advisable that the patient receive some form of therapy—preferably roentgen-ray therapy—rather than none at all. In some cases of eosinophilic granulomatous lesions of the skull, however, there may be extension of the granulomatous process through the dura with invasion of the cerebral cortex and underlying structures. In this case after confirmation by biopsy radical excision of the tumor process from the brain as well as the destroyed portion of the bone certainly should be done, as in other forms of malignant tumors. Extension of eosinophilic granuloma to penetrate the dura, however is not common. If penetration of the dura by this process has occurred it probably can be determined on the basis of the neurologic signs and other means at the time of the original examination. Cranioplasty with the use of a tantalum plate has been employed with good results to cover any large defects of the skull after radical surgical treatment of the lesion and roentgen-ray therapy has been completed.

SUMMARY

In the past decade a clinical entity eosinophilic granuloma, has appeared in the literature and has been accepted by the medical profession for the most part. It is an osteolytic reaction of the flat bones, mostly but it may involve the long bones. It has been known to invade adjacent structures, such as the dura, brain, pleura and other soft tissues. The lesions are best treated by roentgen rays or biopsy and curettage in some cases they have been known to undergo spon-

tanous resolution. If the lesion is not cured, replacement of bone after adequate roentgen therapy can be expected.

Four cases in which eosinophilic granuloma of the skull affected soldiers of the United States Army have been reported with follow-up studies of five years duration.

It is believed that eosinophilic granuloma is a distinct clinical anatomic entity and that it is related to Hand-Schüller-Christian disease and Letterer-Siwe disease. A detailed review of literature and bibliography of the subject are presented.

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THE UROGRAPHIC FINDINGS IN CASES OF TUMOR OF THE SUPRARENAL GLAND

JOSEPH H. KAPLAN AND LAURENCE F. GREENE

VARIOUS roentgenographic techniques have been utilized as diagnostic aids in an attempt to demonstrate changes in contour and an increase in size of the suprarenal gland. Bilateral surgical exploration of the suprarenal gland often is the only means by which the presence or absence of a tumor can be determined.

Cardelli in 1921 developed a technic for radiographic visualization of the renal outline by injecting air into the perirenal spaces. Langeron and his associates in 1929 utilized this principle to visualize a tumor of the suprarenal gland. Since that time Cahill and other authors have revived and used this technic successfully. More recently Wilhelm employed this method in combination with laminography in an attempt to delineate the shadow of the suprarenal gland. Perirenal insufflation however is a procedure that is not without risk.

This survey was undertaken for the purpose of evaluating excretory urography as a diagnostic aid in the detection of tumors of the suprarenal gland. This paper presents the results of a study of seventy two excretory urograms made in cases in which the clinical picture suggested the presence of a tumor of the suprarenal gland. Bilateral surgical exploration of the suprarenal gland was subsequently performed in each case. Downward displacement of the kidney and the presence of a soft tissue mass in the suprarenal region were the two important urographic signs sought for in attempting to confirm a tentative diagnosis of a tumor of the suprarenal gland.

The right kidney is, as a rule, situated at a slightly lower level than the left. Helm made a study of the relative position of the two kidneys in 87 cases. In 57 cases, the right kidney was lower than the left; in 17 cases, the left kidney was lower than the right; in the remaining 13 cases, both kidneys were situated at the same level. The differences in position of the left and right kidney usually varied from 1 to 2 cm., although variations up to 1 to 8 cm. or more have been noted. Moody and Van Nuy, in a study of the position and mobility of the kidneys of healthy young men and women, concluded that the cephalic pole of the left kidney is more often above the twelfth thoracic vertebra than is that of the right kidney. The caudal pole of the right kidney is below the third lumbar vertebra more often than that of the left.

kidney. They also said that the kidneys, like other abdominal viscera, should be recognized as normally "floating viscera" because of the excursions the kidneys make during forced respiration and during the change from the erect to the supine position. An increase in the suprarenal mass would, therefore, be expected to produce a change in the position of the kidney on the corresponding side. In our study an attempt was made to determine the amount of increase in the size of the suprarenal mass that was necessary to produce urographic evidence of displacement of the corresponding kidney.

Seventy-two cases in which there was clinical evidence suggestive of tumor of the suprarenal gland were selected for this study. In each case an excretory urogram was made and bilateral surgical exploration of the suprarenal gland was carried out. In 31 of the 72 cases, excretory urography revealed evidence of renal displacement. In 16 of the 31 cases, excretory urography disclosed unilateral renal displacement and a suprarenal soft tissue mass. In 29 of these cases, the presence of a tumor of the suprarenal gland was confirmed by surgical exploration (Table 1).

The weight of the tumors varied from 53 to 2,685 gm. In 1 case an adrenocortical adenoma which measured 8 mm. in diameter was found in the left suprarenal gland which had been removed. In this case excretory urography disclosed downward displacement of the left kidney. This case however was obviously not included in the group in which positive urographic findings were later confirmed by surgical exploration. In 8 cases in which excretory urography revealed unilateral displacement of the kidney, bilateral surgical exploration of the suprarenal gland did not disclose any evidence of a tumor. Figures 297 to 304 illustrate several instances of renal displacement and the presence of a soft tissue mass in the suprarenal region.

In 30 of the 72 cases, excretory urography did not reveal any evidence of renal displacement or the presence of soft suprarenal tissue. In 10 cases in this group subsequent surgical exploration revealed the presence of a tumor of the suprarenal gland. The smallest tumor had a diameter of 4 mm.; the largest tumor measured 11 by 8 by 7 cm. and weighed 150 gm. In the remaining 20 cases, the exploratory operation revealed that the size, contour, consistency and color of the suprarenal glands were normal (Table 1).

Although this survey is primarily concerned with the urographic findings in cases of tumor of the suprarenal gland, 11 instances of hyperplasia of the suprarenal gland were disclosed by this study. In 2 cases excretory urography revealed the presence of a unilateral mass

of soft tissue and in 1 case it disclosed unilateral renal displacement. The weight of the suprarenal glands varied from 7 to 20 gm. It seems

TABLE 1

UROGRAPHY AND OPEN TIVE FINDINGS IN 24 CASES IN WHICH THE CLINICAL FINDINGS INDICATED THE PRESENCE OF SUPRARENAL TUMOR

Urographic Findings	Surgical Findings		
	Tumor of Suprarenal Gland	N. Tumor of Suprarenal Gland	Hyperplasia of Suprarenal Gland
Evidence of renal displacement	23	8	1
Soft tissue shadow in suprarenal region	18	0	2
No evidence of renal displacement or soft tissue shadow	16	20	8

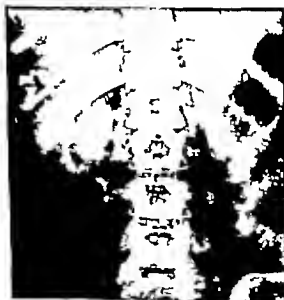


Fig. 227.—Downward displacement of right kidney and soft tissue mass in right suprarenal region due to adrenocortical adenocarcinoma.

reasonable to believe that the mass of soft tissue which was revealed by excretory urography in 2 cases and the unilateral renal displace-

kidney. They also said that the kidneys, like other abdominal viscera, should be recognized as normally "floating viscera" because of the excursions the kidneys make during forced respiration and during the change from the erect to the supine position. An increase in the suprarenal mass would, therefore, be expected to produce a change in the position of the kidney on the corresponding side. In our study an attempt was made to determine the amount of increase in the size of the suprarenal mass that was necessary to produce urographic evidence of displacement of the corresponding kidney.

Seventy-two cases in which there was clinical evidence suggestive of tumor of the suprarenal gland were selected for this study. In each case an excretory urogram was made and bilateral surgical exploration of the suprarenal gland was carried out. In 31 of the 72 cases, excretory urography revealed evidence of renal displacement. In 16 of the 31 cases, excretory urography disclosed unilateral renal displacement and a suprarenal soft tissue mass. In 29 of these cases, the presence of a tumor of the suprarenal gland was confirmed by surgical exploration (Table 1).

The weight of the tumors varied from 33 to 2,683 gm. In 1 case an adrenocortical adenoma which measured 8 mm in diameter was found in the left suprarenal gland which had been removed. In this case excretory urography disclosed downward displacement of the left kidney. This case however was obviously not included in the group in which positive urographic findings were later confirmed by surgical exploration. In 28 cases in which excretory urography revealed evidence of a tumor.

Figures 297 to 304 illustrate several instances of renal displacement and the presence of a soft tissue mass in the suprarenal region.

In 30 of the 72 cases, excretory urography did not reveal any evidence of renal displacement or the presence of soft suprarenal tissue. In 10 cases in this group subsequent surgical exploration revealed the presence of a tumor of the suprarenal gland. The smallest tumor had a diameter of 4 mm; the largest tumor measured 11 by 8 by 7 cm. and weighed 150 gm. In the remaining 20 cases, the exploratory

findings in cases of tumor of the suprarenal gland and of hyperplasia of the suprarenal gland were disclosed by this study. In 2 cases excretory urography revealed the presence of a unilateral mass

of soft tissue and in 1 case it disclosed unilateral renal displacement. The weight of the suprarenal glands varied from 7 to 90 gm. It seems

TABLE 1

UROGRAPHIC VS OPERATIVE FINDINGS IN 78 CASES IN WHICH THE CLINICAL FINDINGS INDICATED THE PRESENCE OF SUPRARENAL TUMOR

Urographic Findings	Surgical Findings		
	Tumor of Suprarenal Gland	No Tumor of Suprarenal Gland	Hyperplasia of Suprarenal Gland
Evidence of renal displacement	29	2	1
Soft tissue shadow in suprarenal region	10	0	2
No evidence of renal displacement or soft tissue shadow	10	90	3



Fig. 297.—Downward displacement of right kidney and soft tissue mass in right suprarenal region due to adrenocortical adenocarcinoma.

reasonable to believe that the mass of soft tissue which was revealed by excretory urography in 3 cases and the unilateral renal displace-



Fig 298—Downward displacement of right kidney and soft tissue mass in right suprarenal region due to pheochromocytoma



Fig 299—Downward displacement of right kidney and soft tissue mass in the right suprarenal region due to tumor of right suprarenal gland, melaninuric type



Fig. 300—Soft tissue mass in left suprarenal region and downward displacement of left kidney due to adenocarcinoma of suprarenal cortex



Fig. 301—Downward displacement of left kidney due to pheochromocytoma



Fig 301—Downward displacement of left kidney due to multiple adrenocortical adenomas.



Fig 302—Downward displacement and torsion of left kidney due to left suprarenal sympathetic.

ment which was revealed in 1 case may be regarded as normal variations. Since hyperplasia of the suprarenal gland is usually found bilaterally, renal displacement would be less evident than it would be in cases of tumors confined to one suprarenal gland. In addition, a hyperplastic suprarenal gland rarely becomes large enough to displace the kidney or to produce a significant soft tissue shadow.



Fig. 304.—Downward displacement and torsion of right kidney due to adenocarcinoma of right suprarenal cortex.

COMMENT

In this study excretory urography was of value in demonstrating the presence of a tumor of the suprarenal gland in 20 of the 30 cases in which a tumor of the gland was removed subsequently. In 10 of the 30 cases in which a tumor of the suprarenal gland was removed surgically, excretory urography failed to reveal any abnormality. In 8 cases in which the urographic findings indicated the presence of a suprarenal tumor, an exploratory operation failed to disclose any tumor. Operation also failed to disclose a tumor in the 20 cases in which the urographic findings were normal.

Excretory urography is a valuable aid in the diagnosis of tumors of the suprarenal gland. The procedure is not hazardous and is less difficult to perform than is perirenal insufflation. Although small cortical adenomas cannot be demonstrated by this method, most tumors of the suprarenal gland will produce urographic changes. The weight of the tumor within certain limits, of course, has no bearing on the degree of renal displacement. In this series of cases, a cortical adenoma of the suprarenal gland which weighed 33 gm. produced urographic evidence of downward displacement of the kidney on the corresponding side but an adenocarcinoma of the suprarenal gland which weighed 150 gm. failed to produce urographic evidence of renal displacement. There was no relationship between the type of tumor and the urographic evidence of a soft tissue mass or renal displacement.

SUMMARY

Excretory urography is valuable as a screening procedure in cases in which the clinical picture suggests the presence of a tumor of the suprarenal gland. Although excretory urography fails to reveal abnormalities in all cases of tumor of the suprarenal gland, urographic evidence of downward displacement of the kidney and of a soft tissue shadow is of diagnostic value in cases in which the clinical findings suggest the presence of a tumor. In cases in which bilateral exploration of the suprarenal gland is contemplated, excretory urography will be of aid in determining which gland should be explored first. In cases in which examination discloses a large abdominal mass in addition to clinical evidence suggestive of a tumor of the suprarenal gland, excretory urography need not be used to localize the tumor.

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DIAGNOSIS IN FOOT PAIN

MARK B. COVENTRY

It has been estimated that 1 out of every 3 persons in the United States consults a shoe salesman, a chiropodist or a physician because of foot pain. This estimate is a challenge to the medical profession. A defeatist attitude toward foot complaints will not benefit the patient. The physician must make a conscientious effort to solve the problem of the patient in this as in all other phases of medicine. Effective therapeutic measures cannot be instituted if the cause of the foot trouble is not determined, and the causes of foot pain are exceedingly numerous. No attempt will be made in this paper to consider all of the causes of foot pain in detail, but certain practical diagnostic points which have been of aid to me and to others in arriving at the proper diagnosis will be given briefly. Excellent monographs covering all details have been written on the foot.^{1, 2, 3}

For practical purposes when the physician takes a history and makes the examination, he should bear in mind the main categories of the conditions which can cause pain.

The conditions which may cause pain of the foot can be classed broadly as (1) developmental, (2) traumatic, (3) neoplastic, (4) vascular and (5) inflammatory and metabolic.

In each of these main groups the findings are characteristic and these make possible the differential diagnosis. Once the condition which is causing pain is grouped in one of these main categories, the cause can be further narrowed down to one of the many subheadings under each main group (Table I).

DEVELOPMENTAL CONDITIONS

The differential diagnosis between the various conditions in this group is made chiefly by examination. The conditions are often manifested in growing children although no complaints may arise until later in life.

Clubfoot.—In cases in which pain in the foot is due to clubfoot, there may be a history of early treatment. Physical examination and the roentgenogram will reveal the deformity. Mild or only partly corrected clubfoot often causes symptoms in later life and these mild conditions are often hard to detect.

Metatarsus Primus Varus.—This condition should always be suspected in an adolescent who has bunions. It is the predisposing cause

of bunions. The foot is broadened and roentgenograms show varus of the first metatarsal bone.

Pes Valgoplplanus.—A flattened longitudinal arch should not always be blamed for all pain in the foot since as many foot complaints arise from too high an arch as from too low an arch. Then too many indi-

TABLE I
CONDITIONS WHICH CAUSE P IN IN THE FOOT

-
- | | |
|-----|--------------------------------------|
| I | Developmental |
| A | Clubfoot |
| B | Metatarsal primus varus |
| C | Pes valgoplplanus |
| D | Pes cavus |
| E | Bunions |
| F | Splay foot or metatarsal levus |
| G | Accessory bones |
| H | Arterio-vascular anomalies |
| II | Traumatic |
| A | Fractures |
| B | Sprains |
| C | Traumatic arthritis |
| D | Plantar neuroma |
| E | Posttraumatic syndrome |
| III | Neoplastic |
| A | Bone tumors |
| B | Soft tissue tumors |
| IV | Vascular |
| A | Occlusive arterial disease |
| B | Chronic venous insufficiency |
| C | Vasospastic disease |
| D | Erythromelalgia, or "burning feet" |
| V | Inflammatory and metabolic |
| A | Rheumatoid arthritis |
| B | Gout |
| C | Cellulitis and lymphangitis |
| D | Periostitis, bursitis and tendinitis |
| E | Osteomyelitis |
-

viduals who have flatfeet do not have symptoms referable to the feet. If pes planus is accompanied by ankle valgus, there is usually more

arch is the cause of the patient's complaints.

Pes Cavus.—A high arch, with prominent heads of the metatarsal

bones, often produces pain, especially on the plantar aspect of the metatarsal heads. A careful neurologic examination should be done for the underlying cause may be myelodysplasia, spastic paralysis or Charcot Marie-Tooth disease. Hammer toes often are found in conjunction with pes cavus and may be the patient's only complaint.

Bunions.—These are easily recognized lateral either to the heads of the first or the fifth metatarsal bone. In the latter position they are referred to as "tailor bunions. A splay foot is often the predisposing cause.

Splay Foot or Metatarsus Latus.—This is a broadening in the region of the metatarsal head and is a frequent cause of foot pain. It is thought to be atavistic. Plantar calluses, bunions and plantar neuromas develop in individuals with splay feet.

Accessory Bones.—These probably account for little pain. Occasionally an accessory navicular bone will rub an adventitious bursa between the shoe and the bony prominence.

Avascular Necrosis.—The cause of this condition is unknown. Kohler's disease is a necrosis of the navicular bone seen in adolescents and is recognized by pain in this region and by evidence of necrosis in the roentgenogram. Freiberg's disease is a similar condition which involves the head of the second and sometimes of the third and fourth metatarsal bones. It, too, produces pain. *Apophysitis of the calcaneus* probably falls in this same group and produces localized pain at the tip of the calcaneus in adolescents.

TRAUMATIC CONDITIONS

The history is important in this group. A story of acute or chronic recurring trauma can usually be elicited. Examination often reveals localized tenderness or pain on motion of the joints. Roentgenograms confirm the presence of bony change.

Fractures.—Of special interest is the march fracture. This usually involves the shaft of a metatarsal bone. There is local pain and often some soft tissue reaction. Initial roentgenograms may not reveal anything abnormal. If the condition is suspected a second set of roentgenograms should be made in two weeks. By that time callus can be seen about a thin, transverse line of fracture if the fracture is present.

Sprains.—The diagnosis is evident from the history and examination.

Traumatic Arthritis.—The history of an old fracture of one or more of the bones of the foot or severe injury is usually elicited in cases in which the pain is due to traumatic arthritis. Pain while walking over

rough ground with less pain when walking on smooth surfaces is almost pathognomonic of traumatic arthritis of a tarsal or ankle joint. Roentgenograms confirm the impression. Pain localized to one of the tarsal joints with limited motion on examination is usually found. The condition known as "hallux rigidus" is a form of traumatic arthritis with secondary hypertrophic changes. It affects the metatarsophalangeal joint of the great toe.

Plantar Neuroma.—The most frequent cause of localized persistent pain between the heads of the third and fourth metatarsal bones is traumatic fibrosis of the plantar nerve with resulting pain. The usual symptoms are severe burning pain on use, with relief on rest or on removal of the shoe and rubbing of the foot. The physician can reproduce the pain by pressing the plantar aspect between the metatarsal heads with the tip of a blunt object.

Posttraumatic Syndrome.—The posttraumatic syndrome is called "painful atrophy of disuse" or "Sudeck's atrophy." This syndrome is characteristically seen after an injury followed by a period of disuse. When this condition is present, the entire foot is tender. The skin is shiny, cold and clammy or may be reddish and actually warmer than normal. Edema may or may not be present. In the later stages roentgenograms show evidence of bone atrophy. This condition should be suspected when chronic pain follows an injury. Paravertebral block of the lumbar sympathetic nerves may be given a therapeutic trial. The pain, coldness and edema will disappear for at least a temporary period after it.

If a similar condition develops in a patient with hypertension who is undergoing thiocyanate therapy, the treatment with cyanate should be discontinued. Hinchey, Hines and Ghormley found that 7 patients at the Clinic who were taking thiocyanates had severe arthralgia of the foot with bone atrophy. The mechanism of development is unknown.

NEOPLASTIC CONDITIONS

Neoplastic lesions of the foot cause pain in the foot in a relatively

usually unilateral and involve a small age group.

Bone tumors.—Bone tumors that may be found in the foot include subungual exostosis, osteochondroma, giant-cell tumor, bone cysts, osteoid osteoma, Ewing's tumor, osteogenic sarcoma and fibrosarcoma.

The presence of pain, usually localized pain plus roentgenographic evidence of the tumor is sufficient basis for the preliminary diagnosis. This then may be confirmed by biopsy.

Soft Tissue Tumors.—Ganglia occur frequently as herniations from the tarsal joints. Cysts of the tendon sheaths along the dorsum of the foot are commonly seen and lipomas, fibromas and xanthomas also occur. Melanomas on the sole of the foot should be recognized and removed early as a high percentage are malignant. Bursae are often present over bony prominences as are corns and calluses. The soft corn is of special interest. Pain between the fourth and fifth toes in the presence of a hyperkeratotic region over a bony prominence should lead to a diagnosis of soft corn—a condition which should be recognized promptly because it produces rather extreme pain and is amenable to treatment. Glomus tumors occur under the nails of the toes and elsewhere. They are exquisitely tender and often appear bluish in color.

Plantar warts are frequent causes of foot pain. When pared down the bed of the corn is often punctured with tiny black dots. They may occur alone or in crops and must be differentiated from ordinary calluses. Radiotherapy is commonly used for plantar warts. Postirradiation skin changes, such as actinic ulcers of the soles of the feet, can be most disabling, and should be looked for.

VASCULAR CONDITIONS

Circulatory conditions account for probably less than 5 per cent of the cases of pain in the foot seen by physicians. But nowhere is the differential diagnosis more important. Serious effects to the patient result from error.

Occlusive Arterial Disease.—A careful history concerning the type of pain usually will make the diagnosis. In both thromboangitis obliterans and arteriosclerosis obliterans claudication is the important factor. A cramping type of pain on use is always suggestive of occlusive arterial disease. In thromboangitis obliterans the pain is often in the arch of the foot for the smaller terminal vessels are occluded first. In arteriosclerosis obliterans the pain is more often in the calf. The age groups are usually different. Both occur more frequently in men.

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NEOPLASTIC CONDITIONS

Neoplastic lesions of the foot cause pain in the foot in a relatively small group of patients. However, when pain is present the physician always should examine the foot carefully for evidence of tumor and roentgenographic examination should always be made. Neoplasms are usually unilateral and involve a wide age group.

Bone tumors.—Bone tumors that may be found in the foot include subungual exostosis, osteochondroma, giant-cell tumor, bone cysts, osteoid osteoma, Ewing's tumor, osteogenic sarcoma and fibrosarcoma.

Gout unlike rheumatoid arthritis is usually monarticular. It affects men in 98 per cent of the cases and in most cases affects the joint of the great toe. It is characterized by acute exacerbations with almost complete remissions and may occur after bouts of overeating or over drinking or after a surgical operation. Hench has pointed out that acute monarticular arthritis occurring within six days after surgical procedures is usually gout. In the later stages of gout tophi may be present and roentgenograms will reveal urate deposits and the more or less typical punched-out appearance of the bone adjacent to the joint. The concentration of uric acid in the blood may not be increased to more than 4.5 or 5 mg. per 100 cc. in the early phases of gout, but later in the course it is usually greater and may be as high as 8 or 9 mg. per 100 cc.

Other forms of acute specific arthritis, such as streptococcal and gonorrheal, must be distinguished from rheumatoid arthritis and gout.

Cellulitis and Lymphangitis.—These are self-evident conditions. Occasionally cellulitis masquerades as acute arthritis or acute gout. Cellulitis of the dorsum or the foot spreading from the base of the toes toward the ankle is a frequent complication of trichophytosis of the toes.

Periostitis, Bursitis and Tendinitis.—These three affections often accompany rheumatoid arthritis. More often they are seen alone. They have the same etiology as similar conditions elsewhere. There is probably a primary unknown metabolic cause for them. They may or may not be accompanied by calcific deposits.

Painful heels, a rather definite syndrome, are usually due to a non-specific, nontraumatic periostitis of the calcaneus. In the course of examination if this condition is present, the physician finds that placing the heel in the hands between the palms and squeezing usually produces exquisite pain. In other cases the pain may be on the tip of the calcaneus at the origin of the plantar fascia. Roentgenograms usually do not reveal any abnormality. Spurs in themselves do not cause pain.

traumatic, in which case an inciting cause can be found by careful questioning. Tendinitis of the Achilles tendon was seen commonly in the army particularly among men who were wearing new boots. Similarly traumatic olecranon bursitis was often observed in men aboard ship who took frequent bridge watches.

Osteomyelitis.—Osteomyelitis takes many forms in the foot, but

Chronic Venous Insufficiency—Varicose veins are more common than flatfeet and varicose veins are blamed for even more foot distress than flatfeet. However varices do not produce pain in the foot. The condition is mentioned only as a warning. A patient should not be promised relief of pain in the foot if the varices are obliterated surgically. The most in the way of symptoms that can be attributed to varices is a feeling of heaviness in the legs and feet. They may of course, produce stasis ulcers.

Vasospastic Disease.—Variations in color or in skin temperature of the toes and foot should suggest Raynaud's disease to the physician. After exposure to cold or after an emotional upset, the toes become pale and cold, and cyanosis frequently occurs. Raynaud's disease is only painful in its extreme forms. The possible coexistence of scleroderma and Raynaud's disease should always be kept in mind during examination. Raynaud's disease occurs usually in women, is bilateral and symmetrical and usually affects both upper and lower extremities.

Erythromelalgia and "Burning Feet."—Erythromelalgia or erythralgia is a rare disease which affects women as a rule. It is characterized by (1) bilateral symmetrical burning pain in the extremities, (2) local increase in skin temperatures, (3) aggravation by exercise and heat and (4) relief by cold and rest. The vessels are patent. It is in some ways similar to chilblains.

The more common, similar affection of the feet is purely subjective and is differentiated by the lack of objective findings. We call it simply "burning feet." It occurs most frequently in middle-aged men. There is a subjective sensation of burning with no evidence of elevation of temperature of the skin. This is a rather common affliction and is seen frequently at the Clinic. The condition is probably a nervous

INFLAMMATORY AND METABOLIC CONDITIONS

The inflammatory and metabolic conditions which affect the foot form a definite group which should be distinguished as causes of pain

women and affects the metatarsophalangeal and tarsal joints. It is usually accompanied by manifestation in other joint of the body. In the chronic phases roentgenographic evidence of bone atrophy or hypertrophic changes may be present. In the chronic form often a lateral deformity of the toes including extreme hallux valgus may be present.

A STUDY OF MALIGNANT TUMORS OF GLANDULAR NATURE FOUND IN THE NOSE, THROAT AND MOUTH*

JOHN R. McDONALD AND FRED Z. HAVENS

Tumors involving the lips or the nasal or oropharyngeal cavities, which are composed of glandular structures have characteristics which differ both clinically and histologically from those of other tumors which are found in the same locations. This study was undertaken in an attempt to show these differences and also to emphasize that one type of tumor cylindroma, is a far more serious disease than generally recognized.

LITERATURE

Many papers have been written regarding glandular neoplasms of nasal paranasal and oral cavities. Most of these however are concerned with reports of individual cases. We are not attempting to compile a complete list of the cases reported.

Lip—Eggers, in 1938 was able to collect data on 64 cases of mixed tumors of the lip from the literature. Only four of these tumors were in the lower lip while the remainder were in the upper lip. Thirty-one (48 per cent) of these mixed tumors had cartilage in them. Hamrick and Howe in 1944 collected reports of seven additional cases of mixed tumor of the lip from the literature.

Tongue.—Glandular neoplasms are of much rarer occurrence in the tongue than in the lip. Brunswick, in 1930 reviewed the existing literature on mixed tumors of the tongue. He was able to collect data on 10 cases from the literature and added one of his own. Five of those in the literature Brunswick regarded as cylindromas. His own case was a mixed tumor. One cylindroma and one mixed tumor (his own) had given rise to metastasis. Lampe in 1942, reported a case of cylindroma of the tongue in which pulmonary metastasis developed although the patient was alive thirteen years after the original diagnosis had been made.

Floor of the Mouth.—It might be expected that mixed tumors would be common in the floor of the mouth, since this is the site of the sublingual salivary glands. However Brunswick, in 1930 was able to collect reports of only two mixed tumors from the literature. He added

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seems to strike the calcaneus and the astragalus bones most frequently. Osteomyelitis may be pyogenic or tuberculous. Pain, redness, heat, swelling and elevated temperature and sedimentation rate and, after the acute phase roentgenographic changes help in making the diagnosis.

Osteomyelitis must be differentiated from Ewing's tumor which it sometimes resembles, osteoid osteoma and march fracture.

COMMENT

The diagnosis in cases of foot pain is often difficult. The physician first should try to catalogue the possibilities that could be responsible for his pain as developmental, traumatic, neoplastic, vascular and inflammatory and metabolic conditions. Once this is done the differential diagnosis becomes easier through a further process of elimination.

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Beck and Guttman in 1936 were able to collect reports of 2 cases from the literature in which the nasal mucosa was involved. Bredlau reported a case of cylindroma of the nose in which there had been symptoms for six years. Following each of two removals, there was prompt recurrence of the tumor. According to Ringertz, nasal adenocarcinomas should be divided into two groups, those which are alveolar and those which are pseudopapillary. In 1945 Ellis reported such a papillary adenocarcinoma in a 12 year old girl. The tumor of the nose was removed surgically and its removal was followed by irradiation. There was no recurrence two years later. A single case of a colloid carcinoma of the nose was reported by Ofner in 1939.

Opinions vary considerably as to the prognosis of glandular neoplasms of the nose. Ringertz was unable to find any reports of metastases from intranasal carcinoma. On the other hand MacComb and Martin found that only 1 of 7 traced patients was alive five years later. They stated that adenocarcinoma of the nose is a radioresistant lesion and must be treated surgically.

Glandular neoplasms also originate in the accessory sinuses. According to New, six of a series of ninety-one primary tumors of the antrum were adenocarcinomas. Hill in 1937 found two adenocarcinomas among eight antral tumors. There is very little in the literature regarding any of the glandular neoplasms in this region except cylindromas. According to Kramer and Som cylindromas occur more frequently in the antrum than in all the other paranasal sinuses combined. Michel, in 1952, after reviewing the literature on tumors of the antrum attempted to show that tumors variously described as cylindromas, endotheliomas, carcinomas and sarcomas are frequently derived from mixed tumors of the parotid type.

There is much confusion regarding mixed tumors and cylindromas. This is true largely because many authors do not agree as to their differentiation. We believe the difficulty to be largely a matter of lack of definition.

Mixed Tumors.—According to Davis, mixed tumors may be defined as "neoplasms of the orofacial region comprised of stroma of mucosal connective tissue often undergoing cartilaginous transformation with groups of epithelial cells which may be either glandular or squamous." Bohme stated that mixed tumors occur ten times more frequently in the parotid than in the submaxillary gland and that the sublingual gland is the site of formation of the mixed tumor in 1 per cent of the whole number. While mixed tumors are common in the

one case of his own (a cylindroma) in which metastases and death had occurred Costa in 1844 reported a cylindroma which had been growing slowly for ten years in the upper jaw of a 54 year old man Four attempts were made at surgical removal but death intervened seven years after the first operation.

Palate.—More mixed tumors have been reported in the palate than in any other single region of the nose mouth and throat Sonnenwchsen in 1929 analyzed data on 92 cases of mixed tumors of the palate and found that fifty tumors occurred in the soft palate and the remainder in the hard palate Rhoads and Mieray in 1937 collected in the literature reports of sixty mixed tumors of the soft palate According to the authors, recurrences of these tumors following surgical removal have been rare There have been many reports of cases since this time which emphasize this fact Very few neoplasms of the palate that have been reported have been classified other than as mixed tumors however Jacques and Florentin reported one cylindroma of the palate

Pharynx and Larynx.—Numerous cases of mixed tumors of the pharynx, nasopharynx, larynx and tonillar regions have been reported including reports of one case each by Ono, in 1934 Peraky in 1935 Goldsmith and Ireland in 1936 Schaudeler in 1937 Fox, in 1939 Craig, in 1941 Lupo in 1942, and Amat, in 1944 Egler in 1942 reported one cylindroma of the larynx A cylindroma of the nasopharynx was reported by Kramer and Som The patient died one year following the diagnosis of the tumor Beck and Guttman in 1938 found 37 cases of cylindroma of the respiratory passages and adnexa, but only one of the larynx The larynx was involved

Fabreant emphasized the rarity of glandular neoplasms in the nose and was able to find only one among twenty-three nasal tumors In a large series of malignant tumors of all kinds in the nasal cavity Ringertz, in 1938, reported data on 10 cases of glandular neoplasm Mixed tumors do not seem to comprise so large a percentage of

hand, Krompecher compared them to basal-cell carcinomas of the skin. Bauer and Fox expressed the belief that these tumors arise from certain cells found in the salivary, lacrimal and mucous glands which are capable of contraction and are called basket or myo-epithelial cells. They suggested the term "adenomyoepithelioma" for this type of tumor. According to Kramer and Som, the following gross features are consistently present in cylindroma: (1) the mucosa is intact over the tumor; if the tumor has originated on a mucous surface; (2) there is a capsule around the tumor; and (3) the cut surface presents a glassy gray appearance.

There has been considerable variance of opinion as to the malignancy of cylindroma. Dockerty and Mayo¹² in a study of tumors of the submaxillary gland found fifteen cylindromas in a group of eighty-one tumors of the submaxillary gland, an incidence of 18.5 per cent. They pointed out that there was more pain associated with cylindromas of the submaxillary gland than with mixed tumors of this gland and that the prognosis was much poorer. In a later communication Dockerty and Mayo¹³ reported 8 cases in which cylindroma had given rise to metastasis. In 1 of these cases the tumor originated in the tongue and metastasis was present in the liver. In the other case the tumor originated in the external auditory meatus and metastasis was found in the lymph nodes of the neck. Stern and Geschickter reported the incidence of cylindromas in the parotid gland as 17.4 per cent of all tumors of the parotid. According to Kramer and Som, cylindromas have a marked tendency to local recurrence. On the other hand, Lemaître stressed the absence of lymphatic involvement. McFarland, and Kramer and Som expressed the opinion that cylindroma is a type of mixed tumor. McFarland suggested that since there was no unanimity of opinion as to what constitutes a cylindroma, it should not be subdivided from the mixed tumor group.

A second form of cylindroma has been recognized by the dermatologists under the term "nevus epitheliomatocylindromatosus." This neoplasm is found only in the skin and is commonly known as "turban tumor." Since its clinical course is quite different from that of cylindromas originating from the salivary glands and mucous membrane, it does not seem logical to regard it as a similar tumor; there-

parotid gland, they cannot be considered uncommon in the mouth and throat and in the lips. It is exceedingly difficult to trace the genesis of these tumors. In an endeavor to explain the presence of the mesothelial and epithelial elements in mixed tumors authors have contended that these tumors originate in various ways. There is, however, no unanimity of opinion as to their origin. Volkmann contended that these tumors are of endothelial origin. Krompecher maintained that they are of epithelial origin and that even the cartilage can be derived from the epithelium by metaplasia; however, this has not been considered satisfactory by most authors. The more commonly accepted view is that the cartilage is derived from branchial cleft elements, a hypothesis which was propounded by Colinbeim. McFarland²⁰ expressed the belief that these tumors originate in sequestered embryonal material and that some of them originate in branchial cleft elements. In a true mixed tumor the prognosis is fairly good. According to McFarland²⁰ the excision of a mixed tumor of the parotid fails in 23 to 30 per cent of the cases, and in 3 per cent recurrence causes death.

Cylindromas.—Cylindroma was first described by Billroth, in 1856. He derived the term "cylindroma" from the histologic appearance of the tumor. He described the tumor as being composed of cylinders of epithelial cells surrounded by cylinders or strands of hyalinized connective tissue. Enclosed within the cylinders of epithelial cells are roundish or oval cavities filled with secretion. According to Lemaitre, this secretion is mucocarmine-positive. In a study of cylindromas found in the tracheobronchial tree, Moersch, Tinney and one of us (McDonald) found that some of the secretion formed by these tumors is mucocarmine-positive while some is not. They suggested that the appearance of the cylinders of epithelial cells with the spaces of various sizes resembles that of Swiss cheese. These tumors have been found in the various salivary glands, in the lacrimal glands, in the upper part of the digestive tract, including the mouth, palate, buccal surfaces, tongue and pharynx, in the upper air passages, including the nasal fossa and accessory sinuses, and in the larynx, trachea and lungs. According to Beck and Guttman they are characterized by "slow growth, local progression, lack of metastases, prompt regression following irradiation and recurrence after local excision."

Volkmann in 1893 expressed the opinion that cylindromas originate from the endothelium of blood and lymph vessels. On the other

logically be suggested that the well-differentiated adenocarcinomas of grades 1 and 2 are in reality mixed tumors in which there is a loss of the mesodermal stroma or in which the glandular elements have overgrown this stroma so that it is no longer apparent. The anaplastic (grades 3 and 4) adenocarcinomas are most frequently found in the nasal cavity where mixed tumor is of rare occurrence, and it seems that these neoplasms have an origin different from that of the mixed tumors.

TABLE 1
LOCATION OF LESION ACCORDING TO PATHOLOGY

Location	Total Cases	Cylindroma	Mixed Tumor	Papillary Adenocarcinoma	Adenocarcinoma	
					Grades 1 and 2	Grades 3 and 4
Floor of mouth	17	7	4	—	5	1
Tongue	15	7	6	1	4	1
Tonsillar region	4	—	1	—	1	2
Palat	66	19	48	—	22	3
Upper jaw	5	2	1	1	—	1
Antrum	29	12	4	2	4	3
Cheek	24	2	10	—	2	1
Nasal cavity	60	15	3	15	12	20
Phary	43	2	21	—	6	3
Nasopharynx	3	4	—	—	2	2
Larynx	5	2	2	—	—	1
Subglottis region	4	2	1	—	1	—
Lips	11	2	3	—	2	2
Miscellaneous	3	2	1	1	3	2
Total	239	66	111	26	80	42

The group of papillary adenocarcinomas is given a separate classification because they present a totally different histologic pattern from that of the other adenocarcinomas found in the anatomic regions under discussion. They are very similar in histologic appearance to papillary adenocarcinoma of the large bowel. Note that 75 per cent of those in our series were found within the nasal cavity.

Cylindroma.—Cylindroma is characterized by slow growth, by its innocuous appearance and by its marked tendency to recur following treatment. A patient who has a well-localized apparently encapsulated tumor may state that this tumor has been present and slowly

written. There have been a few scattered reports of cases belonging to this group, but we have not been able to find any comprehensive reviews.

PRESENT STUDIES

This is a study of 330 cases in which neoplasms of glandular nature were found in the lips or in the nasal, paranasal or oropharyngeal cavities. The group includes all cases seen at the Clinic prior to January 1, 1915. Tissue was available for histologic study in all cases and the classification of these tumors is based exclusively on the histologic appearance. In the main hematoxylin and eosin stains were used. Occasionally other stains such as the mucicarmine stain were employed. The period of survival of patients was calculated from the time of the original histologic diagnosis. In each case, an attempt was made to determine whether or not the patient had a recurrence. This was done either by re-examination of the patient or by evaluation of the patient's description of symptoms or lack of them in a letter. Occasionally it was difficult to determine the exact site of the primary lesion because of the extent of the tumor. In these cases, it was necessary to decide arbitrarily in which region the neoplasm apparently had originated.

The total number of glandular neoplasms as well as their classification into types is given in table 1. It will be noted that these lesions have been found most frequently in the palate, nasal cavity and pharynx. Approximately 28 per cent were found in the nasal or paranasal cavities. The high incidence of cylindroma among the tumors found in the tongue, antrum and nasopharynx is noteworthy.

Forty-one per cent of the tumors of the floor of the mouth were cylindromas. It seems logical to assume that these tumors arose from the sublingual salivary glands. If this is true, it indicates a much higher incidence of cylindroma in the sublingual salivary glands than in other salivary glands. Mixed tumors comprise 75 per cent of glandular

neoplasms and 40 per cent of those in the palate. It is found in the nose and 10 per cent of those in the pharynx. Of the total

number of the glandular tumors found in the nasal cavity

Adenocarcinomas belonging to none of the preceding three types have been divided into two groups: those in which the cells are fairly well differentiated (grades 1 and 2, Broders' method) and those in which the cells are largely anaplastic (grades 3 and 4). It might

importance to the surgeon because although he may remove the tumor without rupturing its capsule recurrence will take place if secondary deposits of tumor are present in the perineural lymphatic tissue of nerve filaments entering or leaving the tumor. We are convinced that this factor is of greater importance in the seriousness of



Fig 303.—Metastatic cylindroma 6½ and ½ years after discovery of primary tumor in floor of mouth. A smaller roentgenogram elsewhere one year previously had revealed extensive pulmonary metastases. The patient's general health was good; the only symptom was slight shortness of breath on exertion.

the disease than is the likelihood of metastasis. Pain or paralysis in a patient who has cylindroma is a symptom the serious import of which should not be overlooked. This symptom suggests perineural lymphatic involvement. Involvement of adjacent bone is also fairly frequent in cylindroma (Fig 303b).

The foregoing statements are emphasized when one examines

enlarging for several years. The lesion may be excised and the surgeon may advise the patient that the tumor has been removed intact without rupturing the capsule and may confidently give a good prognosis, but recurrence often takes place and may persist in spite of extensive and intensive treatment by any and every means available.

If not cured, the disease usually continues to progress slowly and the patient may live for years in reasonable comfort. Twenty-two of our patients who now are dead lived an average of 7.4 years without cure. Eight patients who are still living and who first were treated more than five years ago have survived an average of 9.7 years without cure. One must, therefore, be very wary of considering a patient as cured even after a period of five years following treatment. We have 6 patients living more than five years after treatment with no evidence of recurrence and one who died of other causes after eleven years without recurrence. Six of our patients related that they had been aware of their disease for more than ten years before coming to the Clinic. One patient had known of it for twenty years.

Cylindroma may give rise to metastases, as brought out by Dockerty and Mayo in their study of another group of cases. In the group of cases that we have studied, metastasis occurred in 13 of 86 patients (Fig. 305). The lymph nodes, lungs and bone were involved in that order of frequency.

In histologic studies in connection with this group of cases we have found two types of macroscopic picture. One has been the "Swiss cheese" pattern (Fig. 306a) mentioned earlier and the other has been a tubular pattern (Fig. 306b). In most instances in which the mucous membrane over the tumor has been available for study it was normal in appearance (Fig. 307). Usually the histologic diagnosis can be made with relative ease but occasionally sections from different portions

uniform when only

Fairly frequently tumor cells were found in the lymphatic sinuses around nerves (Fig. 308a). This might have been observed more often if it were not for the fact that most biopsy specimens were obtained

from the

of tumor areas in a manner in which this type of neoplasm spreads. It is of particular

group, but at eight years the reverse is true and only 51 per cent in the cylindroma group are alive while more than 48 per cent of the patients who had adenocarcinomas are alive. A considerable number of patients in the cylindroma group are living, but with recurrences eight years following treatment (Fig. 311). It is noteworthy in the survival curve for patients who had cylindroma that the death rate follows a straight



Fig. 308.—Cylindroma. Involvement of the peritumoral lymphatics, & involvement of adjacent bone.

line downward rather than leveling off after five years as does the curve for practically all other malignant neoplasms. It, therefore, becomes obvious that treatment of cylindroma must be radical. Wide excision or wide destruction by electrocoagulation is recommended if the lesion is of a size and in a location suitable to permit this. Such treatment should be combined with irradiation. Cylindroma is fairly radiosensitive.

If the lesion is not so situated as to permit surgical removal or electrocoagulation, treatment by implantation of radon seeds com-

Figures 300 and 310 and studies the survival rates for patients who had cylindromas as compared with those of patients who had adenocarcinomas.



Fig. 300.—Cylindromas showing the two main patterns—the appearance like that of basal cells, & the neoplasms forming tubules.

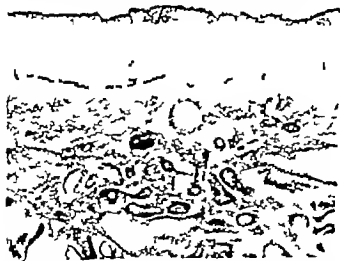


Fig. 307.—Cylindroma. Note the intact tumor capsule over the tumor carcinomas. At the end of five years a greater percentage of patients in the cylindroma group are alive than are alive in the adenocarcinoma

Cylindroma

Per cent survival and per cent symptom free

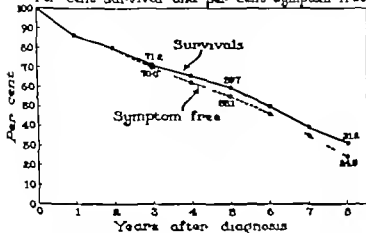


Fig 311 —Cylindroma. Percentage of survival and of patients free of symptoms



Fig 312 —Histological section showing the similarity between the neoplasm and some carcinomas of the colon.

papillary adenocarcinoma (Fig 312) one might suspect that the clinical course would be relatively benign but this is not correct. It is true that the lesion progresses very slowly and seldom gives rise to

bined with roentgen or radium pack irradiation should be given. We have observed that such irradiation has given marked benefit even

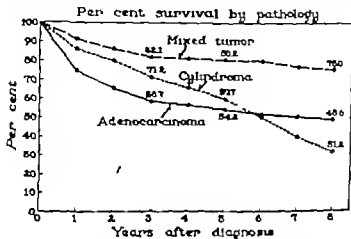


Fig 208—Percentage of survival by type of tumor

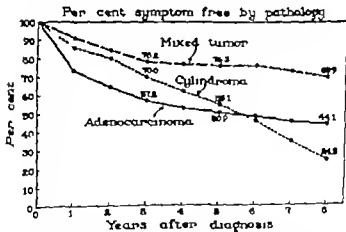


Fig 210—Percentage of patients free of symptoms by type of tumor

in cases in which the disease was incurable by resulting in long periods during which the tumor remained quiescent!

Papillary Adenocarcinoma.—From the cellular picture of the

ing to the Clinic. We have observed metastasis in only four instances among 111 patients who had mixed tumors.

Owing to the tendency of mixed tumors to remain encapsulated the treatment should be by surgical enucleation when possible. Enucleation of a pharyngeal mixed tumor should be preceded by ligation of the external carotid artery. If the tumor has broken through its capsule or if the lines of cleavage had been obliterated by infection or by a previous attempt at removal, electrocoagulation is the treat-



Fig 812.—Mixed tumor showing the epithelial elements which tend to be glandular. The mesodermal element is cartilaginous, as is it is unresistant connective tissue.

ment of preference. Irradiation cannot be expected to be of much value.

Adenocarcinoma Group.—This group probably represents several unrelated types of malignant lesions. It is our feeling that at least some of the adenocarcinomas graded 1 and 2, the well-differentiated adenocarcinomas, are in reality mixed tumors in which the mesodermal element is lacking, however, since they do lack the mesodermal element.

group 3c

Some have

hand, the adenocarcinomas graded 3 and 4 are probably not related

metastases, but when it occurs within the nasal cavity or antrum it may be likened to a fire which smolders unnoticed within the walls of a house. When it finally is recognized it may be beyond control. Patients having such a lesion may notice nasal obstruction and may have what are thought to be polyps removed repeatedly without having the "polyps" sent for microscopic study. Such mismanagement may continue for years (In one of our cases it was fifteen years) and the disease may be incurable when finally recognized. Thornell and one of us (Havens) have pointed this out in another paper.

Such tumors should be approached by a method which will assure adequate exposure of the tumor. Either the fronto-ethmoid or the transnasal type of approach can be used. Irradiation is of little value in the management of these tumors and consequently the growth must be removed completely. We prefer electrocoagulation for this purpose. Our experience in the management of these tumors has been very disappointing. We believe this to be due largely to the fact that in 14 of our 17 cases the lesion was in the nasal cavity and far advanced before the patient came. We had no patient who remained symptom-free for more than five years. Only 5 patients are living, all for periods of less than five years. Three of these are free of symptoms. Metastases was observed to involve the cervical lymph nodes in two instances.

Mixed Tumor.—Possibly we have been unwilling to classify certain lesions as mixed tumor when others might be willing to do so. We have insisted on the presence of two elements namely epithelial elements, usually glandular and myxomatous connective tissue (Fig 313a and b). Squamous epithelium and cartilage are less common components of a mixed tumor but we have not considered these as essential to the diagnosis. These tumors almost without exception have been well encapsulated. It is noteworthy that we have found them in all parts of the nasal and oropharyngeal cavities with the

of survival better for patients who had mixed tumor than it is for patients who had any other of the glandular tumors which we have encountered, but the recurrence rate in the mixed tumor group is much lower. Mixed tumors tend to grow very slowly and to remain encapsulated for long periods. Two of our patients had been aware of the disease for twenty-two and twenty-six years respectively before com-

lesion was demonstrable in the bowel. These two groups of adenocarcinoma do not appear to be related either to the papillary adenocarcinoma or to the cylindroma group.

The low-grade adenocarcinomas within the nasal cavities have resembled the papillary adenocarcinomas in their behavior and in their response to treatment. The growth must be completely removed and for this we prefer electrocoagulation. Irradiation is of doubtful value although it can be expected to be of more value in the treatment of lesions graded 2 than for those graded 1. Among 122 adenocarcinomas, forty-seven were graded 1, thirty-three were graded 2, twenty were graded 3 and twenty-two were graded 4. We have observed five instances among 33 patients in which an adenocarcinoma, grade 2, gave rise to metastasis.

In the treatment of adenocarcinomas graded 3 and 4 it must be kept in mind that they are made up of highly undifferentiated cells, that they tend to progress rather rapidly, that they do not tend to be encapsulated, that they are likely to give rise to metastases and that they are quite radio-sensitive. Treatment is predominantly by means of irradiation, but surgical exploration often is necessary for exposure of the tumor and sometimes electrocoagulation is desirable before the application of radium or the use of roentgen rays.

We have observed 20 patients who had adenocarcinoma classified as grade 3 and 22 patients whose lesions were classified as grade 4. Among the entire group of 42 patients, there were 15 who remained free from recurrence for periods of more than five years after treatment. Twelve of the 15 patients still are living and 7 of them have lived for periods of eight to twenty-two years after treatment (average fourteen years). The one patient of this group who is dead died of other causes after twelve years without recurrence. Five additional patients are free from evidence of recurrence but the length of time since their treatment is less than five years. Evidence of metastases was observed in eight instances.

COMMENT

We have attempted in this study to classify a miscellaneous group

of malignant neoplasms, beginning with the most serious (1) papillary adenocarcinoma, (2) cylindroma (3) adenocarcinoma and (4) mixed tumor. All of these tumors represent examples of malignant neoplasm. All are capable of infiltration and metastasis and all are

to mixed tumor. In many of these the cells are so undifferentiated as to make classification difficult or impossible. Some form mucin,



Fig 314—Mucin-producing adenocarcinoma, grade 1. Note the absence of normal connective tissue or cartilage.



Fig 315—Adenocarcinoma, grade 4. a, the glandular neoplasia is producing spindle cells in stroma. b, signet ring cell adenocarcinoma.

(Figs 315a and b) indeed, in one case there were signet-ring cells resembling those seen in carcinoma of the bowel but no primary

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capable of causing death. Grading does not adequately indicate the serious potentialities of these tumors because the majority of them are composed of well-differentiated neoplastic cells and would therefore be classified as grade 1.

The seriousness of the papillary adenocarcinoma results from the fact that it usually occurs within the nasal cavity and frequently has become very extensive before the diagnosis is made. We believe the seriousness of the cylindroma to be due first, to its innocuous clinical appearance second, to extension of the tumor to the lymphatic tissue in nerve sheaths so that malignant tissue unrecognizable grossly is left when the apparently encapsulated tumor is removed and third to its potentialities for widespread metastasis.

When possible radical operation should be employed in the treatment of the papillary adenocarcinoma, the cylindroma and the adenocarcinomas, graded 1 and 2. For the mixed tumors enucleation of the growth with its capsule intact usually is adequate treatment. For the more highly malignant adenocarcinomas, treatment should be by irradiation, but surgical exploration may be necessary to gain access to the tumor.

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